The Health Effects

of

Involuntary Exposure

to

Tobacco Smoke

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EXECUTIVE SUMMARY

Involuntary (passive or secondhand) exposure to tobacco smoke can be defined as the inhalation of tobacco combustion products other than by directly puffing on a cigarette, cigar or pipe.

Repace and Lowrey (1983), using American survey data on smoking patterns, have estimated that 63% of nonsmokers are passively exposed to tobacco smoke at work and that 86% of nonsmokers are passively exposed to tobacco smoke in either the work or home environment or both. These estimates of passive exposure probably would be higher in Canada because both the proportion of smokers and the average number of cigarettes smoked daily per smoker are higher in Canada than in the United States.

Tobacco smoke can be classified into two general categories - mainstream smoke and sidestream smoke. Mainstream smoke is the smoke which is drawn through the cigarette, cigar or pipe and inhaled by active puffing; sidestream smoke arises from the burning end of the cigarette, cigar or pipe. Most gas and particle phase smoke constituents are in higher concentration in sidestream smoke than in mainstream smoke. About 85% of the smoke to which passive smokers are exposed consists of sidestream smoke. This mixture of 85% sidestream smoke and 15% exhaled mainstream smoke is diluted in the large volume of air in a workplace so that the ambient concentrations of tobacco smoke to which passive smokers are exposed are considerably lower than the concentrations to which active smokers are exposed.

It is difficult to measure accurately the exposure to smoke of passive smokers vis-a-vis active smokers but some attempts have been made based on air sampling and biological monitoring. The air sampling results for various cigarette

smoke constituents in a room where cigarettes are being smoked have been used to estimate the amount of each constituent inhaled by a passive smoker. These results have then been compared to the average concentration of each smoke constituent inhaled by an active smoker and the "cigarette equivalents" due to passive smoking have been calculated. However, the estimated cigarette equivalents derived from such calculations vary considerably depending upon the particular constituent selected. For example under the same exposure conditions, Hugod et al. (1978) estimated the cigarette equivalents per hour to vary from 0.61 based on nitric oxide to 0.02 based on nicotine. For an eight hour workday these estimates would range from 4.88 to 0.16 cigarette equivalents due to passive smoking. The cigarette equivalent estimates also vary with different exposure conditions, making comparison of similar studies difficult. Biological monitoring of blood carboxyhemoglobin, urine, blood and saliva nicotine, and urine and blood cotinine (the major metabolite of nicotine) have also been used to compare exposure from passive versus active smoking. Cotinine is considered a better marker of cigarette smoke exposure than the parent alkaloid nicotine because cotinine has a longer plasma half-life and reaches higher concentrations in plasma and urine making identification easier. These comparisons of various biological monitoring results in active and passive smokers indicate that passive exposure over an eight hour workday in an office environment where many people smoke is probably comparable to light active smoking (ie. about 1-5 cigarette equivalents). Therefore some of the health effects in passive smokers might be predicted by extrapolation from dose-response or dose-effect curves for active smokers.

The principal health effects that have been reported to be associated with passive exposure to cigarette smoke include:

1) irritation of the eyes, nose and throat and the general annoyance associated with these irritant symptoms;

2) exacerbation of pre-existing diseases especially allergic rhinitis, asthma and angina;

3) respiratory symptoms such as cough, increased rates of upper and lower respiratory tract infections and decrements in pulmonary function tests in children exposed to tobacco smoke due to their parents' smoking habits;

4) pulmonary function test changes in adults ($FEF_{25-75\%}$ and $FEF_{75-85\%}$); these changes are indicative of early small airways impairment;

5) lung cancer

There is little doubt about the irritating and annoying effects of secondhand tobacco smoke. A higher percentage of nonsmokers than smokers is annoyed by cigarette smoke. Donahue and Capshaw (1977), in a survey of 9,415 individuals in Pennsylvania, found that 73% of nonsmokers, 66% of exsmokers and 41% of smokers were bothered by tobacco smoke in indoor air. The most frequent irritant symptom reported from exposure to secondhand smoke is usually eye irritation. In a survey by Speer (1968), this symptom was reported in 69.2% of nonallergic individuals. The evidence also appears quite convincing for the exacerbation of the symptoms of some diseases due to passive smoking, especially allergic rhinitis, asthma and angina pectoris. Similarly, the evidence indicates that in children increased frequency of pulmonary symptoms such as chronic cough and increased

rates of acute respiratory infection, as well as decrements in various pulmonary function tests are associated with exposure to parental (mainly maternal) smoking. The existing research on changes in pulmonary function tests ($FEF_{25-75\%}$ and $FEF_{75-85\%}$) indicative of small airways impairment in adults exposed passively to cigarette smoke for many years is more equivocal, but on balance seems to favour the occurrence of such changes.

The question of whether cancer, especially lung cancer, is caused by involuntary exposure to tobacco smoke has been intensely investigated since the original paper by Hirayama (1981). Overall, the evidence from published epidemiologic studies does suggest that a small increased risk of lung cancer may be associated with long-term exposure to secondhand tobacco smoke. This conclusion is also biologically plausible given the proven association between lung cancer and active smoking, the demonstrated presence of several carcinogens, including lung carcinogens in sidestream tobacco smoke, and the general acceptance that the risk of lung cancer is directly related to the amount of tobacco smoke inhaled.

Therefore, various health effects have been demonstrated to be due to involuntary exposure to tobacco smoke. However the health hazard to an individual or a group of individuals in a particular work environment would depend on the actual exposure conditions. These exposure conditions are a function of a number of factors such as the size of the room, the ventilation rate, the percentage of fresh make-up air supplied, the number of smokers in the room, the total number of cigarettes smoked, the rate and manner of smoking and the type of cigarettes. Although it is difficult to quantify the health hazard on an individual basis, it is recommended that long-term exposure to secondhand tobacco smoke in the workplace should be minimized or avoided.

INTRODUCTION

According to Collishaw and Mulligan (1984), Canada has the highest rate of cigarette consumption per capita of any industrial nation. The United States Department of Health and Human Services (1984) estimated that, in 1980, smokers made up 34% of the adult population in the United States. The average consumption per smoker was 22 cigarettes a day. Collishaw (1983) stated that in Canada in 1981 both the percentage of smokers (39%) and the average daily consumption of cigarettes per smoker (27) were higher. He estimated that there were 7.4 million smokers in Canada in 1981 and a total yearly cigarette consumption of 74 billion cigarettes.

However active smoking is not the only way in which one can be exposed to tobacco smoke. Involuntary (passive or secondhand) smoking is the result of the inhalation of combustion products of tobacco other than by directly puffing on a cigarette, cigar or pipe.

Repace and Lowrey (1983), using American survey data on smoking patterns, have estimated that 63% of nonsmokers are passively exposed to tobacco smoke at work and that 86% of nonsmokers are passively exposed to tobacco smoke in either the work or home environment or both. Because a higher percentage of Canadians than Americans smoke and the consumption per smoker is greater in Canada, the probability of nonsmokers being exposed passively to cigarette smoke at work and/or at home, and the intensity of their exposure, probably would be expected to be at least as great in Canada as in the U.S.

The major health effects from active smoking - lung and other types of cancer, chronic obstructive lung disease, coronary artery disease - have been investigated in

considerable detail and a compilation of research was provided in the report by the U.S. Surgeon General in 1979. However, concern about the health effects from passive smoking is comparatively recent. Given the large percentage of nonsmokers passively exposed to cigarette smoke at work and/or at home, the demonstration of clinically important health effects in nonsmokers would constitute an important public and occupational health problem.

EXPOSURE CONDITIONS

Physiochemical Characteristics of Cigarette Smoke

Cigarette smoke consists of liquid particles dispersed in a gas medium. The particulate phase is defined as that portion of smoke retained by a Cambridge (standard) filter; the gas portion passes through the filter. Each liquid particle is composed of many organic and inorganic chemicals and the particles vary in diameter from about 0.2 to 1.0 microns. Holbrook (1983), in a recent review of the physiochemical characteristics of cigarette smoke, mentions that although cigarette smoke constituents are usually classified as being gaseous or particulate, individual constitutents may be in either phase or they may exist in a distribution equilibrium and hence be found in both phases.

Many factors influence the chemical composition of cigarette smoke including the type of tobacco, the physical design of the cigarette and the smoker's puffing characteristics. During puffing, temperatures in the burning end of the cigarette reach 900°C while the temperature at the butt end is near 30°C. The high temperature of combustion results in pyrolysis and pyrosynthesis and the generation of more than 3,800 identified chemicals in cigarette smoke.

Tobacco smoke can also be classified into two general categories - mainstream smoke and sidestream smoke. Mainstream smoke is the smoke which is drawn through the cigarette by active puffing. This mainstream smoke is filtered by the smoker's upper respiratory tract and lungs (if inhalation occurs) and is then exhaled into the general environment. Sidestream smoke arises from the burning end of the cigarette, cigar or pipe and enters directly into the environment. Sidestream and mainstream smoke differ in the concentration of various tobacco combustion products due mainly to the temperature of combustion and the filtration by the cigarette. Most gas phase and particulate phase constituents are in higher concentration in sidestream smoke than in mainstream smoke as indicated in Table 1. In particular the concentrations of various carcinogens such as 2-naphthylamine, aniline, benzo(a)pyrene and pyrene are greater in sidestream smoke than mainstream smoke. Most (up to 85%) of the smoke in a room results from sidestream smoke.

Relative Exposure to Tobacco Smoke Constituents from Passive Versus Active Smoking

The mainstream and sidestream concentrations of various tobacco smoke combustion products do not reflect accurately the true exposure of the involuntary smoker in comparison to the active smoker. The mainstream smoke inhaled by the active smoker directly enters the respiratory tract and lungs and is diluted only by the volume of air breathed in by the smoker while inhaling. The mixture of approximately 85% sidestream smoke and 15% exhaled mainstream smoke to which the passive smoker is exposed is diluted in a much larger volume of air. Therefore passive smoking results in a quantitatively smaller smoke exposure than active smoking.

TABLE I

Major Toxic Agents in Cigarette Smoke;
Ratio of Concentrations in Side Stream Smoke (SS)
to Mainstream Smoke (MS)

Gas Phase	Mainstream smoke/cigarette				SS/MS		
Carbon dioxide	10	-	80	mg			8.1
Carbon monoxide	0.5	-	26	mg			2.5
Nitrogen oxides (NO)	16	-	600	µg	4.7	-	5.8
Ammonia	10	-	130	µg	44	-	73
Hydrogen cyanide	280	-	550	µg	0.17	-	0.37
Hydrazine			32	µg			3
Formaldehyde	20	-	90	µg			51
Acetone	100	-	940	µg	2.5	-	3.2
Acrolein	10	-	140	µg			12
Acetonitrile	60	-	160	µg			10
Pyridine			32	µg			10
3-Vinylpyridine			23	µg			28
N-Nitrosodimethylamine	4	-	180	ng	10	-	830
N-Nitrosoethylmethylamine	1.0	-	40	ng	5	-	12
N-Nitrosodiethylamine	0.1	-	28	ng	4	-	25
N-Nitrosopyrrolidine	0	-	110	ng	3	-	76

Particulate phase	Mainstream smoke/cigarette				SS/MS		
Total particulate phase	0.1	-	40	mg	1.3	-	1.9
Nicotine	0.06	-	2.3	mg	2.6	-	3.3
Toluene			108	µg			5.6
Phenol	20	-	150	µg			2.6
Catechol	40	-	280	µg			0.7
Stigmasterol			53	µg			0.8
Total phytosterols			130	µg			0.8
Naphthalene			2.8	µg			16
1-Methylnaphthalene			1.2	µg			26
2-Methylnaphthalene			1.0	µg			29
Phenanthrene	2.0	0	80	ng			2.1
Benz(a)anthracene	10	-	70	ng			2.7
Pyrene	15	-	90	ng	1.9	-	3.6
Benzo(s)pyrene	8	-	40	ng	2.7	-	3.4
Quinoline			1.7	µg			11
Methylquinoline			6.7	µg			11
Harmane	1.1	-	3.1	µg	0.7		2.7
Norharmane	3.2	-	8.1	µg	1.4		4.3
Aniline	100	-	1200	ng			30
o-Toluidine			32	ng			19
1-Naphthylamine	1.0	-	22	ng			39
2-Naphthylamine	4.3	-	27	ng			39
4-Aminobiphenyl	2.4	-	4.6	ng			31
N-Nitrosonornicotine	0.2	-	3.7	µg	1	-	5
NNK*	0.12	-	0.44	µg	1	-	8
N-Nitrosoanatabine	0.15	-	4.6	µg	1	-	7
N-Nitrosodiethanolamine	0	-	40	µg			1.2
Polonium-210	0.03	-	0.5	pCi	N/A		

* NNK = 4 (Methylnitrosamino) - 1 - (3-pyridyl) - 1 - butanone
Source: U.S. Department of Health, Education and Welfare (1979).

The involuntary smoker's exposure is determined by the concentration of tobacco combustion products in the ambient air. The ambient concentration is influenced by many factors including the size of the room, the ventilation rate, the percentage of fresh make-up air supplied, the number of smokers in the room, the total number of cigarettes smoked, the rate and manner of smoking and the type of cigarettes. Therefore, it is difficult to quantify accurately the exposure to secondhand tobacco smoke although attempts have been made based on air sampling and biological monitoring.

Hugod et al. (1978) measured the airborne concentration of various gas phase and particulate phase components in sidestream cigarette smoke. The smoke was generated in a room with a volume of 68.1 m^3 by a smoking machine. Initialy, 20 cigarettes were "smoked" by machine for 10 minutes resulting in an air concentration of CO of 20 ppm. The CO concentration was kept at this level by the machine smoking of a further 30 cigarettes during the 3-hour experimental period. For each contaminant the amount inhaled (mg/h) by passive exposure could be estimated by multiplying the airborne concentration of each contaminant by 0.4 (0.4 m^3 was taken to be the average volume of air inhaled by a man at rest during a one-hour period). This allowed the amount of each contaminant inhaled by active and passive smoking to be compared and cigarette equivalents per hour (CE/h) and cigarette-equivalent-time (CET) to be calculated.

Cigarette equivalents per hour (CE/h) is a conventional way of expressing the amount of a particular component of tobacco smoke inhaled by passive smokers relative to the amount of the same component inhaled by the active smoker from one cigarette. Cigarette-equivalent-time (CET) expresses the time in hours for which a person has to stay in a room with a particular atmospheric composition to inhale the same amount of each tobacco smoke constituent as the average cigarette smoker inhales with mainstream smoke

from one cigarette.

The values of CE/h and CET obtained by Hugod et al. are presented in Table 2.

Table 2

Average Yield from Mainstream Smoke Inhaled by a Smoker (mg/cigarette)	Inhaled Amount by Passive Smoking (mg/h)	CE/h	CET (h)
NO	0.30	0.182	0.61	1.6
CO	18.40	9.16	0.50	2.0
Aldehyde	0.81	0.21	0.26	3.8
Acrolein	0.09	0.01	0.14	7.1
TPM*	25.30	2.300	0.09	11.1
Nicotine	2.10	0.041	0.02	50.0
Cyanide	0.25	0.005	0.02	50.0

* Total Particulate Matter

The results indicate that an individual must be involuntarily exposed to secondhand cigarette smoke for two hours to inhale the same amount of CO as is inhaled by the active smoking of one cigarette; the corresponding figure for hydrogen cyanide is 50 hours. The large differences in CET and CE/h for different contaminants indicate the dependence of these estimates on the particular tobacco smoke constituent chosen for active/passive smoking comparison. Furthermore, comparison of CE/h or CET values based on air contaminants depends on the exposure conditions in a specific study and this makes comparisons between studies difficult. For example, Russell et al. (1973) in a study in which the exposure concentrations of CO were approximately twice those in the study by Hugod et al. (1978) reported a CE/h for CO of about 1.0 compared to the value of 0.5 obtained by Hugod et al.

Several studies have attempted to use biological monitoring results such as carboxyhemoglobin and urine nicotine in passive smokers vis-a-vis active smokers to estimate the cigarette equivalents due to passive exposure to tobacco smoke for a specified time period. For example, Seppanen (1977) studied the carboxyhemoglobin levels of nonsmokers passively exposed to cigarette smoke (carbon monoxide concentration of about 30 ppm) and concluded that the mean increase of carboxyhemoglobin extrapolated over an eight-hour period would be approximately equivalent to the exposure obtained from actively smoking about five cigarettes. Feyerabend et al. (1982) studied nicotine concentrations in the urine and saliva of 82 smokers and 56 nonsmokers after a morning at work. In this study the passive exposure occurred under actual work conditions during the morning of a typical working day. All nonsmokers were found to have measurable amounts of nicotine in both saliva and urine. The amount of nicotine absorbed by nonsmokers produced salivary and urinary concentrations similar to those found in light smokers. Light smokers were described as workers who had smoked up to three cigarettes in the three to four hours prior to the urine and saliva nicotine measurements. Foliart et al. (1983) reported that passive absorption of nicotine from tobacco smoke by flight attendants during a transoceanic flight was roughly equivalent to absorption after smoking one cigarette.

The half life of blood carboxyhemoglobin is approximately four hours. Thus, blood carboxyhemoglobin is a useful biologic marker of recent exposure to secondhand tobacco smoke but it cannot be used to assess long term exposure. Similarly, the half-life of nicotine in the blood of smokers is quite short. Armitage et al. (1975) found that the half life of nicotine in arterial blood following inhalation ranged from 24 to 84 minutes with a mean of about 40 minutes. Most of the absorbed nicotine is metabolized rapidly with the liver being the major site of detoxification; cotinine is the major metabolite of nicotine. Recently cotinine has come to be considered a

better marker of cigarette smoking than the parent alkaloid because it has a longer plasma half-life (about 30 hours) and reaches higher concentrations in plasma and urine making identification easier. Also cotinine is found in only trace amounts in tobacco smoke; this makes contamination of urine samples with exogenous cotinine very unlikely (in contrast to nicotine).

Matsukura et al. (1984) measured urine cotinine levels in 392 smokers and 472 nonsmokers and examined the relationship between urinary cotinine excretion in the nonsmokers and the "smokiness" of their environment. The urinary cotinine levels of nonsmokers who lived with smokers were higher than those of nonsmokers who did not, increasing with the combined daily cigarette consumption of smokers in the family. Nonsmokers who lived with smokers who smoked more than 40 cigarettes per day had urine cotinine levels (mean ± SEM of 1.56 ± 0.57µg per mg of creatinine) which were nearly identical to those of smokers of less than 3 cigarettes per day. The urinary cotinine values of nonsmokers who worked with smokers were also higher than those of nonsmokers who did not, and the urine cotinine values in nonsmokers increased with the number of smokers in the workplace. The presence of smokers in both the home and the workplace also increased the cotinine levels. These findings of detectable quantities of cotinine in the urine of nonsmokers exposed passively to cigarette smoke at home and/or at work were consistent with previous studies indicating the presence of nicotine in the plasma, urine and even saliva of nonsmokers passively exposed to tobacco smoke.

These comparisons of various biological monitoring results in active and passive smokers, indicate that passive exposure over an eight hour workday in an office environment where many people smoke is probably comparable to light active smoking (ie. about 1-5 cigarette equivalents). Therefore, some of the health effects anticipated in passive smokers might be estimated by extrapolation to low doses from dose-response or dose-effect curves for active smokers.

HEALTH EFFECTS

General Overview

The principal health effects that have been reported to be associated with passive exposure to tobacco smoke include:

1) irritation of the eyes, nose and throat and the general annoyance associated with these irritant symptoms;

2) exacerbation of pre-existing diseases especially allergic rhinitis, asthma and angina;

3) respiratory symptoms such as cough, increased rates of upper and lower respiratory tract infections and decrements in pulmonary function tests in children exposed to cigarette smoke due to their parents' smoking habits;

4) pulmonary function test changes in adults ($FEF_{25-75\%}$ and $FEF_{75-85\%}$); these changes are thought to be indicative of early small airways impairment;

5) lung cancer.

The scientific and medical literature linking each of these five categories of health effects with passive smoking will now be reviewed.

Irritation and Annoyance

The results of several surveys have indicated that a large percentage of both smokers and nonsmokers are annoyed by involuntary exposure to tobacco smoke. A telephone survey of individuals in the U.S. conducted by the United States Department of Health, Education and Welfare (1975) indicated that 77% of male and 80.5% of female nonsmokers found it annoying to be near a person who is smoking cigarettes; for current smokers, the corresponding figures were 35% of the

males and 34.5% of the females. Donahue and Capshaw (1977) carried out a survey of 9,415 residents of Southwestern Pennsylvania; they found that 73% of nonsmokers, 66% of ex-smokers and 41% of smokers were bothered by tobacco smoke in indoor air. A survey in Toronto by Shephard and LaBarre (1976) of more than 1,000 citizens showed that 75% of the nonsmokers were annoyed by tobacco smoke in restaurants and 53% in offices.

In a survey of 472 office employees in Switzerland by Weber and Fischer (1980) the results of the answers to the question "Does smoke disturb you at work, at home, in public means of transport, in restaurants?", are indicated in Table 3.

Table 3

Answers to the question: "Does smoke disturb you at work, at home, in public means of transport, in restaurants?"

Number of Employees = 472

Place	Yes (%)	No (%)
Workplace	62	38
Home	63	37
Public means of transport	58	42
Restaurants	54	46

Speer (1968) carried out a questionnaire survey to determine the specific symptoms incurred by individuals passively exposed to cigarette smoke. The subjects included 250 nonallergic and 191 allergic individuals. The allergic group included some individuals under active treatment who had reported adverse effects from exposure to tobacco smoke

and was therefore not a random sample. The symptoms reported by the allergic and non-allergic individuals are summarized in Table 4.

The most frequently reported symptom was eye irritation for both allergic (73.3%) and nonallergic (69.2%) subjects. This reporting of eye irritation as the most prevalent symptom from passive exposure to cigarette smoke has been corroborated by other studies.

In the study by Weber and Fischer (1980) mentioned earlier, extensive air sampling was carried out as well as the administration of a questionnaire on irritation and annoyance to 472 office employees.

These employees came from seven different companies and worked in a total of 44 different workrooms. Air samples for CO, NO, NO_2 and particulate matter (PM) (particle size 0.01-10 µm) were collected in 40-liter teflon bags over a one-hour period and analyzed in a mobile laboratory. Due to the smaller airborne concentrations of nicotine a longer sampling duration of three hours was required. The nicotine was collected by passing the office air through a Cambridge filter (44 mm. diameter) at a flow rate of 17.6 liters/minute and extracted with a mixture of diethyl ether/methylene chloride (1:1) making use of an ultrasonic bath; analysis for nicotine was carried out by high resolution gas chromatography.

TABLE 4

Reactions to Tobacco Smoke as Reported by 191 Allergic Nonsmokers and 250 Nonallergic Nonsmokers from Speer (1968)

	Allergic Patients					
	Boys*	Men	Girls*	Women	Total	%
Number of Patients	38	44	29	80	191	100.0
Eye irritation	30	32	22	56	140	73.3
Nasal symptoms	25	31	22	59	137	67.1
Headache	6	22	9	50	87	46.0
Cough	20	13	19	35	87	46.0
Wheezing	9	13	8	13	43	22.5
Sore throat	4	13	6	21	44	23.0
Nausea	3	5	3	18	29	15.2
Hoarseness	1	9	1	20	31	16.0
Dizziness	0	2	1	8	11	5.3
	Nonallergic Patients					
	Boys*	Men	Girls*	Women	Total	%
Number of Patients	19	71	21	139	250	100.0
Eye irritation	9	54	14	96	173	69.2
Nasal symptoms	5	28	2	38	73	29.2
Headache	5	26	5	43	79	31.6
Cough	7	15	10	31	63	25.2
Wheezing	1	4	0	6	10	4.0
Sore throat	0	7	0	7	14	5.6
Nausea	3	6	0	14	23	9.2
Hoarseness	0	6	0	5	11	4.4
Dizziness	2	2	2	10	16	6.4

* Under 16 years

At the same time as they were taking indoor measurements, the authors determined the outdoor concentrations of CO, NO and NO_2 to control to some extent the possible influence of outdoor air pollution on indoor air pollution. For each contaminant the difference values D (D = indoor concentration minus outdoor concentration) represented approximately the concentration due to air pollution generated inside the room. Also, between 4:00 a.m. and 6:00 a.m. the authors obtained measurements of the pollutant concentrations in unoccupied rooms. The difference values Δ (Δ = indoor concentration in the occupied room minus indoor concentration in the unoccupied room) gave information about the influence of smoking (as well as other office activities) on the air quality.

The results of the air sampling for CO, NO, NO_2, PM and nicotine are summarized in Table 5.

Table 5

Air Pollution in the Workrooms. Mean Values of all Measurements, Standard Deviations, and Maxima
Adapted from Weber and Fischer (1980)

	Unit	N	$\bar{x}$	S.D.	Maximum
CO	ppm	490	2.8	1.6	8.9
NO	ppb	492	84	80	450
NO_2	ppb	492	60	25	200
PM	$\mu g/m^3$	489	170	133	1,130
Nicotine	$\mu g/m^3$	160	1.1	2.1	16.0
ΔCO	ppm	353	1.1	1.3	6.5
ΔNO	ppb	348	32	60	280
ΔNO_2	ppb	354	4	22	115
ΔPM	$\mu g/m^3$	429	133	130	962
ΔNicotine	$\mu g/m^3$	140	0.9	1.9	13.8
$_D$CO	ppm	485	0.8	1.1	6.2
$_D$NO	ppb	487	22	48	320

Δ-values = difference: outdoor concentration minus control (unoccupied room)

D-values = difference: indoor concentration minus outdoor concentration

Maximum: 1-hour values for CO, NO, NO_2, PM; 3-hour value for nicotine

N = number of air samples

The corresponding exposure limit guidelines for each contaminant according to the ACGIH TLV 1984-85 booklet are as follows:

Contaminant	Exposure Limit TWA	STEL
CO	50* ppm	400 ppm
NO	25 ppm	35 ppm
NO_2	3 ppm	5 ppm
PM (respirable particulate)	5 mg/m^3	
Nicotine	0.5 mg/m^3	

* 35 ppm in Ontario

Therefore, none of the concentrations of the airborne contaminants exceeded the corresponding ACGIH exposure limit guidelines. Furthermore, assuming additive (in this case irritant) effects for NO, NO_2, PM and nicotine still does not result in the TLV for the mixture being exceeded.

However, these exposure limit guidelines are established to minimize the occurrence of various health effects in workers exposed in industry on a repeated basis. They are probably not appropriate criteria for determining the comfort of office workers or for estimating the health consequences due to passive cigarette exposure in an office environment. The correlation coefficients for the air sampling results of the different pollutants from the study by Weber and Fischer (1980) are summarized in Table 6.

Table 6

Correlation Coefficients between Different Pollutant Concentrations (absolute values)

	NO	NO_2	PM	Nicotine
CO	0.83	0.75	0.42	0.39
NO		0.76	0.24	0.45
NO_2			0.24	0.63
PM				0.41

The correlation coefficients for the Δ values (indoor concentration minus indoor concentration in an unoccupied room) of the air sampling results of the different pollutants are summarized in Table 7.

Table 7

Correlation Coefficients between Different Pollutant Concentrations (Δ Values = Indoor Concentration Minus Concentration in an Unoccupied Room)

	ΔNO	ΔNO_2	ΔPM	ΔNicotine
ΔCO	0.73	0.55	0.33	0.01
ΔNO		0.66	0.12	0.01
ΔNO_2			0.23	0.36
ΔPM				0.39

In general, relatively good correlations were obtained between the gas phase components (CO, NO, NO_2), but the correlations of the gas phase components with the particulate phase components (PM, nicotine) and the correlations between the particulate phase components were relatively low.

The results of the interviews of office employees were also compared to the air sampling results. The frequency of reported specific complaints of irritation and annoyance in workrooms with low and high ΔCO, Δnicotine and ΔPM are summarized in Table 8.

Table 8

Results of the Questionnaire on Subjective Complaints Related to Rooms with Low and High ΔCO, ΔNicotine and ΔPM Levels

	Complaints		
	Air Quality Rated as "Bad"	"Sometimes or Often Disturbed by Smoke"	Sometimes or Experience Eye Irritation"
Air Sampling in Workroom			
ΔCO (ppm)			
<1.4	18%	35%	24%
>1.4	42%**	46%	30%
ΔNicotine ($\mu g/m^3$)			
<0.2	20%	35%	25%
>0.2	41%**	46%*	28%
ΔPM ($\mu g/m^3$)			
<150	22%	38%	24%
>150	43%**	45%	30%

* $P < 0.05$

** $P < 0.01$ (X^2 - test)

In the workrooms with high ΔCO, Δnicotine, and ΔPM airborne concentrations, more employees evaluated air quality with regard to smoke as "bad"; similarly the percentages of people disturbed by smoke and suffering eye irritation was increased. Thus, the reported annoyance and irritation could be explained to some extent by air pollution due to tobacco smoke.

However when Weber and Fischer calculated the correlation coefficients between the mean pollutant concentrations of each of the 44 workrooms and the corresponding frequency of reported specific complaints of irritation or annoyance, the correlations were in general quite low. These are summarized in Table 9.

Table 9

Correlation Coefficients between the Mean Pollutant Concentrations in Each Room and the Corresponding Frequency of Complaints of Irritation or Annoyance

	Air Quality Rated as "Bad"	"Sometimes or Often Disturbed by Smoke"	"Sometimes or Often Experience Eye Irritation"
ΔCO	0.10	0.46**	0.21
ΔNicotine	0.22	0.10	-0.08
ΔPM	-0.02	0.10	0.08

** $P<0.01$

These results indicate a poor correlation between mean pollutant concentrations in each room and the frequency of specific complaints of irritation or annoyance. Therefore, although broad strata of ΔCO, Δnicotine and ΔPM are fairly good predictors of irritation or annoyance (Table 8), as the strata become narrower (Table 9) the predictive validity of

these air sampling results for such health effects in exposed employees diminishes. Such poor correlations do not allow for easy extrapolation to no-effect levels.

However, these poor correlations between air sampling results and health effects may be explained in part by the method of air sampling. The samples were all area samples collected over a one-hour period for CO, NO, NO_2 and PM and a three-hour period for nicotine. In each room 12 samples were obtained during 2 days. Therefore, the time weighted average results of these samples (weighted according to the duration of the sampling period) may not reflect the true irritating or annoying peak exposures to secondhand tobacco smoke. Also area samples are not as representative of actual employee exposure as personal samples.

This field study, although providing comprehensive data on air sampling and the relation of the air sampling results to irritation and annoyance in exposed employees, still did not allow for accurate and precise assessment of the relation between the degree of air pollution from passive smoking and the associated irritation or annoyance. The standardized conditions of laboratory experiments in a climatic chamber are probably more appropriate for this purpose.

Weber et al. (1979) and Muramatsu et al. (1983) have carried out a number of exposure chamber studies to evaluate the relationship between various air contaminants from passive smoking and different outcomes such as annoyance and eye irritation. These studies have been summarized recently by Muramatsu et al. (1983). In these exposure chamber studies the smoke was produced by a smoking machine and the concentrations of various contaminants (CO, NO, NO_2, PM) generated in the exposure chamber were measured. In order to assess only the contaminant concentrations due to tobacco smoke, the background levels of each contaminant (measured before smoke production) were deducted from the

concentrations measured during smoke production. These differences were again referred to as ΔCO, ΔNO, ΔNO_2, and ΔPM. Irritant symptoms and general annoyance in the exposed subjects were assessed by a questionnaire. The results of these studies in terms of the relationship between the most frequently reported symptom (eye irritation) and the contaminant with the best correlation with this symptom (ΔCO) were summarized by Muramatsu et al. (1983). His summary is presented in Table 10. The relationship between ΔCO and eye irritation is more obvious when these results are presented in the form of a graph (Figure 1).

Table 10 and Figure 1 show that there is a marked increase from 2% to 10% in the incidence of "strong and very strong" eye irritation between the smoke levels corresponding to 1.3 and 2.5 ppm ΔCO.

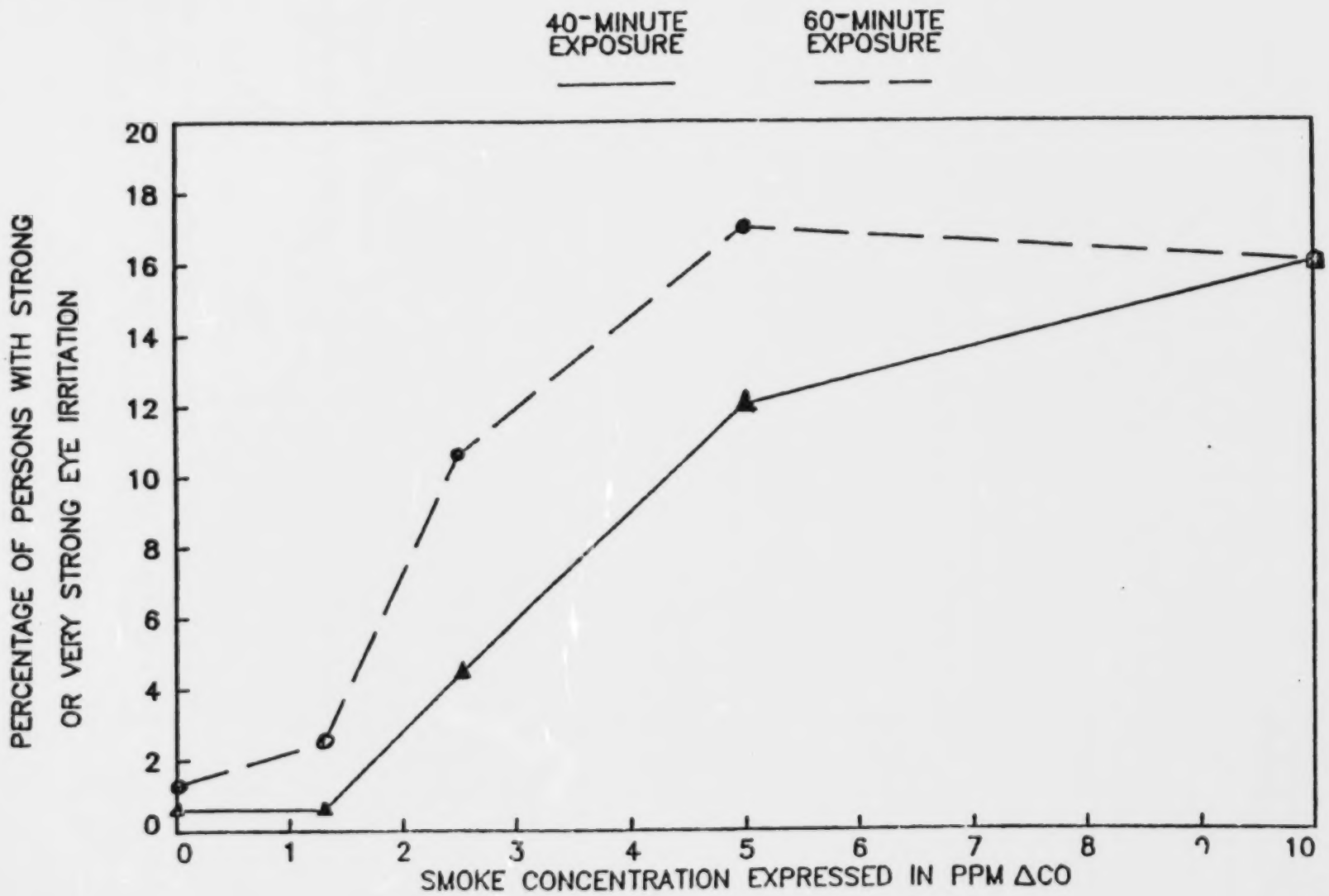
Table 10

The Percentage of Subjects Showing
Eye Irritation from Passive Exposure to
Cigarette Smoke
(Exposure Chamber Studies)

Experiment	Exposure Duration (Min)	Eye Irritation (%) Moderate	Strong and Very Strong
0 ppm ΔCO*	40	1.9	0.6
	60	2.5	1.3
1.3 ppm ΔCO*	40	9.4	0.6
	60	12.5	2.5
2.5 ppm ΔCO	40	13.8	4.4
	60	17.5	10.6
5 ppm ΔCO**	40	23	12
	60	15	17
10 ppm ΔCO***	40	25	16
	60	28	16

* = 40 subjects, ** = 32 subjects, *** = 43 subjects

FIG 1 EYE IRRITATION FROM PASSIVE SMOKING



Muramatsu et al. also pointed out that these levels of 1.3 to 2.5 ppm ΔCO are achieved by the presence of only a few smokers in a work environment. For example Weber (1981) has shown that ΔCO levels above 1.3 ppm are reached when two cigarettes are smoked per hour during a working day in a naturally ventilated room of 80 m^3 with one air change per hour.

Exacerbation of Pre-Existing Disease

A number of studies have investigated the effect of passive exposure to tobacco smoke on individuals with pre-existing diseases that might increase susceptibility to tobacco smoke. These studies have dealt mainly with allergic rhinitis, asthma and angina.

Allergic Rhinitis

While some investigators recently have suggested the existence of an allergy to certain glycoprotein constituents of cigarette smoke, others maintain that a specific respiratory allergy to cigarette smoke has yet to be demonstrated. An entire chapter of the 1979 U.S. Surgeon General's Report on Smoking was devoted to the subject of allergy and tobacco smoke. The conclusion reached was that the existence of an allergy to tobacco smoke has not been definitely established but that individuals with a history of allergies to other substances are more likely to report the irritating effects of tobacco smoke. However, it is uncertain if this is a psychological rather than a physiological response. Speer (1968) compared symptoms from exposure to tobacco smoke in 250 nonallergic nonsmokers and 191 allergic nonsmokers whose allergies included nasal allergy, allergic headache and/or asthma. Eye irritation was experienced about equally; however nasal symptoms were experienced with passive exposure to tobacco smoke by 61% of the allergic subjects and by only 29% of the nonallergic subjects. The frequencies of other symptoms among these two groups of allergic and nonallergic subjects, respectively,

were as follows: headache (46% versus 32%), cough (46% versus 25%), wheezing (23% versus 4%), sore throat (23% versus 6%) and hoarseness (16% versus 4%).

Shephard et al. (1979) carried out a study in which a questionnaire relating to symptoms from secondhand tobacco smoke exposure was completed by 426 adults attending the offices of ophthalmologists in the Toronto area. Among those respondents with hay fever there was a more than two fold increase in the frequency of rhinorrhea due to involuntary exposure to tobacco smoke compared to individuals without hay fever.

Weber and Fischer (1980) also found that employees suffering from hay fever reported significantly more eye irritation at work from involuntary exposure to tobacco smoke than those without hay fever.

Hence it appears that the symptoms of allergic rhinitis are exacerbated by passive cigarette smoke exposure.

Angina Pectoris

Aronow (1978) carried out a randomized crossover study which provided evidence that exposure to passive smoking decreases the time to the development of angina in exercising patients. Ten subjects with stable angina pectoris were each exposed to either no smoking, smoking in a well ventilated room or smoking in an unventilated room. The 10 subjects were randomized to the order of presentation of the three exposure conditions. The subjects sat with three volunteers who, during the passive smoking exposure conditions, each smoked 5 cigarettes over a 2-hour period. When the room was well ventilated there were 11.4 air exchanges per hour.

Before and after each exposure the subjects were exercised on a bicycle ergometer until the onset of angina pectoris and the duration of exercise was recorded with a stopwatch.

The results indicated that in comparison to no involuntary exposure to tobacco smoke, when the subjects were passively exposed to 15 cigarettes smoked within two hours in a well ventilated room or an unventilated room, there was a statistically significant increase in resting heart rate, systolic and diastolic blood pressure and venous carboxyhemoglobin and a significant decrease in heart rate and systolic blood pressure at the time angina occurred. For all of these outcomes the changes were more pronounced from involuntary exposure to tobacco smoke in an unventilated room.

The carboxyhemoglobin concentrations averaged 1.20% and 1.30% before smoke exposure during periods simulating good and poor room ventilation, respectively. With smoke exposure, mean carboxyhemoglobin levels rose to 1.77% with good ventilation and 2.28% with poor ventilation. The duration of exercise until angina was decreased 22% after passive smoking in a well ventilated room ($P<0.001$) and decreased 38% after passive smoking in an unventilated room ($P<0.001$).

Therefore the author concluded that under the conditions of this experiment, passive smoke exposure during exercise caused anginal pain to develop more quickly.

Anderson et al. (1973) earlier demonstrated that the duration of exercise before onset of anginal pain in patients with angina pectoris was significantly shortened after exposure to 100 ppm CO as well as 50 ppm CO, compared with air. In this study the CO exposure was provided by breathing a CO and air mixture with a face mask for 4 hours.

Therefore it is likely that the CO component of secondhand tobacco smoke is mainly responsible for shortening the exercise time to angina in the patients in the Aronow study. Actually Aronow attributed this effect to CO and nicotine; he also speculated that other components of tobacco smoke may have been involved including oxides of

nitrogen and hydrogen cyanide and possibly psychologic factors produced by the experimental conditions.

In the studies by Aronow and Anderson et al., the shortening of time to angina was associated with small increases in carboxyhemoglobin. The mean carboxyhemoglobin level in the subjects exposed passively to smoking in an unventilated room in the study by Aronow was only 2.28%. In a review of the Adverse Health Effects of Smoking and the Occupational Environment by NIOSH (1979) it is stated that "studies have shown that carboxyhemoglobin levels in excess of 5% can cause cardiovascular changes which are dangerous for persons with coronary heart disease (CHD)". Exercise reduces the level at which carboxyhemoglobin concentration is associated with anginal symptoms in individuals with CHD. The Report by the Surgeon General in the U.S. (1979) concluded that there is evidence that elevations in carboxyhemoglobin levels capable of being produced by involuntary smoking can reduce the exercise duration for induction of angina in some individuals with CHD.

Other cardiovascular health effects aside from angina pectoris have been associated with passive smoke exposure. A recent report by Sinzinger and Kefalides (1982) suggests that passive exposure to cigarette smoke is associated with decreased platelet sensitivity to the antiaggregatory prostaglandins (E_1, I_2, D_2). A decrease in platelet sensitivity to these prostaglandins is a determinant of hemostatic regulation and thus may be responsible for early changes preceding atherosclerosis. These changes in platelet sensitivity found after passive smoking, especially in nonsmokers, suggest an increased risk of CHD in nonsmokers exposed to tobacco smoke for long periods of time. However, the demonstration of the association of this risk factor with secondhand smoke exposure needs to be corroborated by additional studies. Furthermore, the association of passive smoking with this risk factor does not indicate a causal association of passive smoking with CHD.

Aronow et al. (1974) demonstrated a significant reduction in the time to development of leg pain due to intermittent claudication in 10 subjects with angiographically documented occlusive arterial disease when the subjects were exposed to 50 ppm of CO for 2 hours. The CO was breathed from a tank through a mask and hence this experiment was similar to the experiment by Anderson et al. (1973) on the effect of CO on angina pectoris. However the exacerbation of intermittent claudication symptoms has not been demonstrated under natural or more realistically simulated passive smoking conditions.

Bocanegra and Espanoza (1981) reported two cases of Raynaud's phenomenon in passive smokers. In both cases the individuals were exposed to the same heavy chain smoker ($4\frac{1}{2}$ packages of cigarettes a day) and their symptoms disappeared when the exposure was reduced. Given this evidence the authors suggested that passive exposure to tobacco smoke should be added to the list of conditions associated with Raynaud's phenomenon. However, although these case studies are suggestive, they do not provide sufficient evidence at present to justify a causal relationship between passive smoking and Raynaud's phenomenon.

Asthma

There is evidence from population surveys that some symptoms in asthmatics such as wheezing are precipitated by passive exposure to tobacco smoke. Shephard et al. (1979) carried out a survey in which a questionnaire relating to symptoms from involuntary exposure to tobacco smoke was completed by 426 adults attending the offices of ophthalmologists in the Toronto area. Irrespective of smoking habits (non-smoker, ex-smoker, active smoker), wheezing in a cigarette smoke contaminated atmosphere was approximately twice as common in asthmatics (25.0%) as in non-asthmatics (11.8%). In a second study Shephard et al. (1979) compared symptoms in asthmatics and non-asthmatics after passive exposure to cigarette smoke for 2 hours. The subjects sat in a 14.6 m^3

room and cigarette smoke was generated by a smoking machine. Prior to exposure four cigarettes were machine-smoked simultaneously followed by combustion of one further cigarette at 30 minute intervals. Wheezing was reported in 43% of the asthmatic subjects and in 10% of the nonasthmatic subjects; in addition the proportion of subjects reporting tightness in the chest was noticeably greater in asthmatics than nonasthmatics (43% versus 5%).

O'Connell and Logan (1974) assessed the effects upon asthmatic children if parents stopped smoking cigarettes. They reported improvements in 18 of 20 asthmatic children; in contrast, only four of 15 asthmatic children improved when their parents continued to smoke.

There is conflicting evidence as to whether passive smoke exposure per se results in an acute worsening of pulmonary function test results in asthmatics. Dahms et al. (1981) compared pre and post exposure pulmonary function test results (FEV_1, FVC, $FEF_{25-75\%}$) in 10 patients with bronchial asthma and 10 healthy control subjects exposed to smoke from a smoke generator in an environmental chamber. The smoke was produced from cigarettes (15 mg of tar and 0.15 mg of nicotine) smoked with a 30 ml puff volume at one puff per minute to a butt length of 30 mm. Asthmatic and control subjects showed the same increase in carboxyhemoglobin as a result of the exposure - about 0.40%. The asthmatic group demonstrated a significant decrease in pulmonary function during this exposure. After one hour of involuntary exposure to smoke FEV_1 decreased 21.4% ($P<0.01$) and FVC decreased 20% ($P<0.01$) in the asthmatic patients. One asthmatic patient had an audible wheeze after 60 minutes of exposure. The control subjects showed no significant change in pulmonary function when exposed to secondhand cigarette smoke.

These results suggest that nonsmokers with bronchial asthma are at risk when exposed to secondhand cigarette smoke, but because the exposure conditions were evident to the

subjects, the authors were not able to exclude the possibility that these changes in pulmonary function in asthmatics were caused by a psychological or emotional reaction to cigarette smoke rather than to cigarette smoke exposure per se.

Shephard et al. (1979) in a similar study subjected 14 asthmatic subjects to a two-hour exposure to cigarette smoke in a closed room of 14.6 m^3 capacity. Prior to exposure four cigarettes were "smoked" in a smoking machine followed by combustion of one cigarette at 30 minute intervals thereafter. Preliminary studies established that with this pattern of combustion a CO concentration of 24 ppm above ambient was developed and sustained. The initial suspended particulate concentration was greater than 4 mg/m^3 but values dropped to about 2 mg/m^3 over the two-hour exposure period. Subjects were randomized to the order of exposure to either smoke or to ambient air without smoke in the same room and pre and post exposure pulmonary function tests were obtained. No significant differences in the changes in FEV_1, $Vmax_{50\%}$ or $Vmax_{25\%}$ were observed between the smoke and no smoke exposure periods. Therefore these results differ from those of Dahms et al. (1981). When these two studies are compared, the exposure conditions appear similar. The major difference is probably the way in which the patients were selected. In the study by Dahms et al., five of the ten patients were included because they reported complaints when exposed to cigarette smoke. Furthermore, the methacholine inhalation challenge tests done on these 10 subjects indicated that this group of asthmatic patients was quite sensitive to methacholine. Five of the asthmatic subjects responded with a 20% decrease in FEV_1 (threshold criterion) with the lowest dose of 0.075 mg/ml in the nebulizer; one responded at 0.15 mg/ml, two at 0.62 mg/ml and two at 1.25 mg/ml. The dose required for confirmation

of asthma is 25 mg/ml, a value considerably above that for anyone in Dahms' group of asthmatic patients. In contrast the 14 subjects in the study by Shephard et al. consisted of volunteers attending an asthma class. Therefore, the subjects in the study by Dahms et al. appear to have been more sensitive to methacholine and probably cigarette smoke than the subjects in Shephard et al.'s study. This may have contributed to the different results in the two studies.

To summarize, asthmatic individuals may experience exacerbation of some asthmatic symptoms such as wheezing when exposed passively to cigarette smoke. However, studies designed to demonstrate pulmonary function test changes in asthmatic subjects passively exposed to cigarette smoke have produced equivocal results. Possibly such changes are limited to a subgroup of asthmatics who are especially sensitive to tobacco smoke. This increased sensitivity is probably related to nonspecific irritation of "twitchy" airways or a psychological reaction to the smell and/or sight of cigarette smoke rather than to a specific allergy to tobacco smoke components.

Individuals with chronic obstructive lung disease other than asthma (e.g. chronic bronchitis, emphysema) represent another group who may be particularly susceptible to involuntary exposure to cigarette smoke. Aronow et al. (1977) exercised 10 patients with hypoxic chronic lung disease before and after a one-hour exposure to 100 ppm CO. There was a significant reduction in the mean exercise time until marked dyspnea from 218.5 seconds to 146.6 seconds after exposure to CO. This study has not yet been repeated with exposure consisting of involuntary smoking rather than inhalation of 100 ppm CO. Hence, it has yet to be determined to what extent these results by Aronow et al. of increased dyspnea due to CO exposure in individuals with chronic obstructive lung disease can be generalized to individuals with similar lung diseases involuntarily exposed to tobacco smoke in the work environment.

Pulmonary Effects In Children

A number of studies have investigated the effects of parental smoking on the respiratory health of children.

Cameron et al. (1969) were the first to suggest a relationship between the prevalence of childhood respiratory illness and parental smoking habits. They conducted two telephone surveys of Detroit families. In the first survey (1969) they found a statistically significant relationship between the prevalence of reported respiratory infection in children and parental smoking habits when all children under age 16 were considered. In a larger survey of the same city (1973) they also found a relationship between parental smoking and prevalence of respiratory illness in the 10-16 and birth-5 year age subgroups. Neither study controlled for socioeconomic status or smoking by the children (which might have been a factor in the 10-16 year age group). However, the data suggested an increase in prevalence of respiratory disease in children from passive exposure to cigarettes smoked by their parents.

Colley (1974) also reported an increased prevalence of respiratory illness in children from passive smoke exposure due to parental smoking. In this study an increased prevalence of cough in children aged 6-14 years whose parents smoked was found; however this association lost its significance when parental cough and phlegm production were taken into account. Therefore, Colley felt that parental smoking was causing parental cough and phlegm production which in turn increased the likelihood of infection in the children.

Subsequently, Colley et al. (1974) published the results of a study showing that in children in the first year of life,

but not in the second to fifth year, prevalence of cough was significantly higher in those whose parents smoked. This excess was still significant if the analysis was restricted to those parents who did not have phlegm. The rate of respiratory infection increased with the number of smokers and the number of cigarettes smoked per day in the home and as mentioned, was independent of parental symptoms as well as social class and birth weight.

A study by Leeder et al. (1976) demonstrated an increased prevalence of bronchitis, pneumonia and wheeze in the first year of life in children whose parents smoked. Subsequent studies suggested that not only wheezing (Weiss et al., 1980) but also frank asthma (Gormaker et al., 1982) in young children appeared to be more prevalent if the parents smoked. A number of other studies have also provided evidence that the prevalence rates of various respiratory symptoms and illnesses in young children are affected by parental smoking habits (Said et al., 1978; Taylor et al., 1979; Tager et al., 1979; Bonham et al., 1981; Hasselblad et al., 1981; Gormaker et al., 1982; Tager et al., 1982; Docker et al., 1982; Schenker et al., 1982).

Colley et al. (1973) found that respiratory symptoms in early adult life were related to early childhood respiratory illness. The prevalence of cough was studied in 3,899 twenty year olds and the prevalences of various independent variables possibly contributing to the cough were also determined. Of these independent variables, current cigarette smoking was found to have the greatest effect on symptom prevalence, followed by a history of a lower respiratory tract illness contracted prior to age two. Therefore, the increased rates of pulmonary symptomatology and illnesses associated with involuntary exposure to tobacco smoke in childhood could have long term consequences in terms of increased prevalence of pulmonary symptoms in adult life.

Several studies have investigated the relationship between pulmonary function tests in children and involuntary smoking in the home. The results of some of the more important and carefully designed studies are presented in Table 11. As indicated in the table several studies have found a significant association between various pulmonary function test results and passive smoking (Weiss et al., 1980; Tager et al., 1979; Hasselblad et al., 1981; Lebowitz, 1982; Ware et al., 1983). However, other studies have failed to demonstrate this association (Shilling et al., 1977; Lebowitz and Burrows, 1976; Dodge, 1982; Speizer et al., 1980). In some studies such as those of Weiss et al. (1980) and Tager et al. (1979) there was a dose-response relationship in that the level of pulmonary function in children was inversely related to the number of smokers in the home. Usually, when analyzed by multiple regression, maternal smoking habits had the greatest impact on the pulmonary function of the children. Younger children were usually more adversely affected than older children. However, several investigations carried out in warm, dry areas of the U.S. (such as the studies by Lebowitz and Burrows (1982) and Dodge (1982) in Arizona) have failed to find an association between pulmonary function test changes in children and parental smoking habits. Probably children in these climates spend less time indoors and are less exposed than children in more northern climates to cigarette smoke generated by their parents' smoking habits. Also, all of these studies lack quantitative estimates of involuntary exposure to tobacco smoke aside from crude indexes such as whether or not the parents smoke or the parents' daily cigarette consumption. Hence, there may be large differences in involuntary exposure to tobacco smoke in the various studies. This factor, as well as differences in the age distributions and size of the sample cohorts and the pulmonary function tests utilized, probably are the main reasons for the discrepancies in the results of different studies. Nevertheless, the demonstration of decrements in pulmonary function tests in children exposed passively to cigarette smoke in several different studies indicates that

for some children (mainly young children i.e. < 2 years) under specific exposure conditions (northern climate, poor general ventilation in the home) such decrements in pulmonary function tests occur due to involuntary exposure to tobacco smoke.

These pulmonary function tests have included FEV_1, FVC and various flow rates. The demonstration of an association between decrements in pulmonary function test results, particularly the flow rates, in children exposed passively to tobacco smoke may increase the plausibility of similar pulmonary function test changes in adults exposed chronically to secondhand tobacco smoke. This is germane to the occupational environment because a recent study by White and Froeb (1980) has found changes in flow rates in adults exposed passively to cigarette smoke in the work environment.

Table 11

Pulmonary Function in Children and Adults Exposed to Involuntary Smoking
Adapted from Weiss et al. (1983)

Author	Population and Age Range	Pulmonary Function Measure	Outcome	
Schilling et al. (1977)	816 children 7 to 17 yrs. of age in Connecticut and South Carolina	FEV_1 as per cent predicted	No effect of parental smoking	
Tager et al. (1979)	444 children 5 to 19 yrs. of age in East Boston, MA	MMEF in standard deviation units	Significant effect of parental smoking	
Weiss et al. (1980)	650 children 5 to 9 yrs. of age in East Boston, MA	MMEF in standard deviation units	Significant effect of parental smoking	
Vedal and associates (1983)	4,000 children 6 to 13 yrs. of age	FEV_{175}, FVC_1 $Vmax_{50}$, $Vmax_{75}$, $Vmax_{90}$	FVC positively associated, flows negatively associated	Flows showed dose response with amount smoked by mother
Lebowitz and Burrows (1976)	271 households with complete smoking histories of both parents and pulmonary function of children aged >6, Tucson, AZ	FEV_1, FVC_1 $Vmax_{50}$, $Vmax_{75}$ derived from MEF_1V curves, expressed as standard deviation units	No effect of parental smoking	
Dodge (1982)	558 children 8 to 10 yrs. of age in AZ	FEV_1 by age change FEV_1/H^3 per year	No effect of parental smoking	

(Table 11 cont'd)

Author	Population and Age Range	Pulmonary Function Measure	Outcome	
Hasselblad et al. (1981)	16,689 children 5 to 17 yrs. of age, 7 geographic regions in U.S.	$FEV_{.75}$ as per cent predicted	Significant effect of mother's smoking, but not father's smoking	
Speizer et al. (1980)	8,120 children 6 to 10 yrs. in 6 U.S. cities	FVC and FEV_1 as per cent predicted	No effect for FEV_1 or FVC	
Ware et al. (1983)	10,000 children 6 to 11 yrs. of age in 6 U.S. cities	FEV_1 and FVC	FVC positively associated with smoking, FEV_1 negatively associated	FEV_1 showed dose response with amount smoked by mother

Chronic Respiratory Effects In Adults

White and Froeb (1980) carried out a cross-sectional analytic survey to evaluate the effect of passive smoking on pulmonary function in 2100 middle-aged subjects. These subjects were selected from a large group of individuals undergoing evaluation during a "physical fitness profile" course. Smoking habits were assessed from a self-administered questionnaire and the subjects were classified into various active-passive smoking categories; the results of pulmonary function tests were compared in these different active-passive smoking categories. Those passively exposed to cigarette smoke at work not only scored significantly lower on the $FEF_{25-75\%}$ and $FEF_{75-85\%}$ pulmonary function tests than nonsmokers not passively exposed at work, but were found to be in the same state of impaired performance as those individuals who had smoked 1-10 cigarettes per day for more than twenty years. This was true for both men and women. No differences in FVC or FEV_1 were found in the passive smokers compared to the "true" nonsmokers.

In the presence of normal FVC and FEV_1, reduced forced mid-expiratory ($FEF_{25-75\%}$) and end-expiratory ($FEF_{75-85\%}$) flow rates are thought to be indicative of small airways impairment. Therefore this study suggested that passive exposure to cigarette smoke in the work environment can cause small airways impairment in both men and women. Kauffman et al. (1983) carried out a similar study to assess the effect on pulmonary function of passive exposure to cigarette smoke in the home. These authors used data from the French Cooperative Study PAARC (Pollution Atmospherique et Affections Respiratoires Chroniques). The primary purpose of the PAARC study was to look at the possible effect of air pollution on respiratory symptoms and ventilatory function. A total of about 3,800 individuals

were included in the study of the effects of passive smoking on pulmonary function. Nonsmokers were divided into (a) "true" nonsmokers defined as those living in households with no smoker or ex-smoker and (b) passive smokers defined as those living with at least one smoker or ex-smoker. However those nonsmokers living with an ex-smoker were excluded from the analysis. In the whole nonsmoking group, FEV_1, FVC and $FEF_{25-75\%}$ were all not significantly different for true nonsmokers and passive smokers for both men and women. Restricting the comparison to subjects aged 40 or more (eg. those presumably exposed for at least 15 years), the difference in $FEF_{25-75\%}$ for true nonsmokers versus passive smokers became significant for both men and women. FEV_1 and FVC values were also significantly different for true nonsmokers versus passive smokers in women. After adjustment for sociocultural variables (social class and educational level) the differences in $FEF_{25-75\%}$ for men and FEV_1 and $FEF_{25-75\%}$ for women were still significant. Also adjustment for air pollution (SO_2 concentration) or number of people in the household did not change the differences observed between true nonsmokers and passive smokers in either sex. A higher percentage of passive smokers than true nonsmokers reported a history of asthma (17.2% vs. 7.8%). This unequal distribution of asthma in the groups compared could have confounded the relationship between passive smoking and pulmonary function test results. When these asthmatic subjects were excluded, the difference in $FEF_{25-75\%}$ between true nonsmokers and passive smokers was of borderline significance for men (P=.07); exclusion of those subjects with a history of asthma did not modify the results for women. Separate adjustment was carried out for the various potential confounders mentioned above. However, simultaneous adjustment for these covariates or potential confounders by, for example, the use of multiple linear regression was not done. This simultaneous adjustment would have been preferable and would have allowed for a more unbiased and precise comparison of passive smokers versus

true nonsmokers. Because of the larger size of the female compared to the male passive smoking group, only females were analyzed for dose-effect relationship between passive smoke exposure and pulmonary function test results. In the group of women without paid work, whose main passive exposure to cigarette smoke would probably be more closely related to their husbands' smoking habits than it would be for working women, a statistically significant (P=.025) dose-effect relationship between $FEF_{25-75\%}$ and the amount of tobacco smoked by their husbands was demonstrated. However, statistically significant dose-effect relationships were not found for FEV_1 and FVC. In summary, this study by Kauffmann et al. found that for nonsmoking subjects of either sex passively exposed to cigarette smoke in the home environment the $FEF_{25-75\%}$ was significantly lowered compared to true nonsmokers. Therefore these results tend to corroborate those of White and Froeb (1980). However, in this study the index of secondhand smoke exposure was the spouses' smoking habits and the passive smoking occurred in the home; in White and Froeb's study the passive exposure took place at work. Also the dose-effect relationship demonstrated between $FEF_{25-75\%}$ and passive exposure to tobacoo smoke in the large subgroup of women without paid work provides further evidence for a causal relationship between second-hand smoke exposure and $FEF_{25-75\%}$ decrement.

However, the results of other studies have not confirmed the findings of White and Froeb (1980) and Kauffmann et al. (1983). Comstock et al. (1981) compared the rates of pulmonary symptoms and clinically important changes in pulmonary function tests in 1,724 residents of Washington County, Maryland who were classified according to active and passive exposure to cigarette smoke. The frequency of major respiratory symptoms (eg. chronic cough, wheezing, etc.) showed no evidence of an association with passive exposure to cigarette smoke at home. Also, the comparison of pulmonary function test results indicated that, although in each smoking category (never smokers, exsmokers, current

smokers) there was a definite tendency for subjects with passive exposure to cigarette smoke in the household to have impaired ventilatory function, none of the observed differences achieved statistical significance. Impaired ventilatory function was defined as an FEV_1 less than 80% of the predicted value or less than 70% of the FVC.
Shilling et al. (1977) investigated the contribution of familial factors, including smoking by parents to lung function and respiratory symptoms in the parents and their children. A total of 376 two-parent white families were included in the study. The analysis included a comparison of pulmonary symptoms and pulmonary function test results in adults with active and/or passive exposure to cigarette smoke. Passive exposure to cigarette smoke was taken to be the presence in the household of an actively smoking spouse. The results indicated that the prevalence of pulmonary symptoms such as cough, phlegm production and wheezing in nonsmokers was unrelated to whether or not their spouses smoked. Similarly, the FEV_1 results in nonsmoking women were not related to passive exposure to tobacco smoke due to their spouses' smoking habits. In nonsmoking men the FEV_1 results were lower in those whose wives smoked compared to those whose wives did not smoke. However, when these men were further subdivided by their past smoking history, the men who never smoked did not deviate significantly from normal; the male ex-smokers in the group had particularly low lung function. Therefore, the authors concluded that passive smoking was not an important factor affecting lung function or pulmonary symptomatology in adults in this study.

To summarize, of the four key studies that have investigated the relationship between passive smoke exposure and pulmonary function test changes, two have demonstrated an association (White and Froeb, 1980 and Kauffmann et al. 1983) and two have not (Comstock et al. 1981 and Shilling et al. 1977).

All four studies utilized an essentially similar design architecture - that of the cross-sectional analytic survey. As such none of the studies was truly prospective.

The studies differed in the following main areas:

1) Age of the study groups

In general the subjects in the Comstock et al. and Shilling et al. studies were younger than the subjects in the White and Froeb and Kauffmann et al. studies; hence the average duration of involuntary exposure to tobacco smoke was less for the subjects in the two studies that failed to demonstrate an association between passive exposure to tobacco smoke and pulmonary function test decrement. The study by Shilling et al. included parents with young children; the study by Comstock et al. included subjects starting at age 20. Conversely, the subjects in White and Froeb's study were middle aged and, for those who smoked or were passively exposed to cigarette smoke, the duration of exposure was 20+ years. Kauffmann et al. found no significant effect in pulmonary function test results in subjects passively exposed to cigarette smoke when considering the whole PAARC population including young subjects. Differences were only observed in those subjects aged 40 years and over. Hence, a certain duration of exposure appears necessary before an effect on pulmonary function test results can occur due to secondhand smoke exposure. The two studies that did not demonstrate an association

between passive smoke exposure and pulmonary function test decrement did not have mean durations of exposure for the subjects in their cohort as long as the two studies which demonstrated such an association.

2) The choice of pulmonary function test

$FEF_{25-75\%}$ and $FEF_{75-85\%}$ are more sensitive indicators than FEV_1 or FVC of early small airways impairment. Shilling et al. and Comstock et al. considered only FEV_1; indeed Comstock et al. used a qualitative variable derived from FEV_1 which was even less sensitive than FEV_1 in terms of detecting early small airways impairment. Both the studies by White and Froeb and Kauffmann et al. used pulmonary function test outcomes that included FEF rates.

Therefore the two studies that demonstrated an association between pulmonary function and passive smoking used more appropriate or sensitive outcomes than the two studies with negative results.

Based on these two key criteria - the duration of exposure of the cohorts to secondhand smoke and the sensitivity of the outcome variable to demonstrate an effect from involuntary exposure to tobacco smoke, the studies by White and Froeb and Kauffmann et al. appear methodologically superior to the other two studies. Therefore, the literature supports the occurrence of subtle changes in FEF rates due to passive exposure to tobacco smoke in the home environment or at work. However, these findings still should be corroborated by additional studies.

Assuming that these changes in FEF rates are caused by involuntary exposure to tobacco smoke, the next question

is the clinical importance of such changes. In particular, what is the likelihood of subsequent severe pulmonary disease such as chronic obstructive pulmonary disease (COPD) given the presence of these small changes in FEF rates in middle aged subjects after approximately 20 years of involuntary exposure to tobacco smoke?

Niewoehner et al. (1974) carried out a case control autopsy study comparing lung histologic findings in young smokers and nonsmokers who had experienced sudden non-hospital deaths. The characteristic lesion observed in young smokers (mean age 25 years ± 1.6 years SEM) was a respiratory bronchiolitis; this lesion was rarely seen in nonsmokers and the difference in the distribution of this lesion in smokers versus nonsmokers was statistically significant ($p<.002$). The authors postulated that this respiratory bronchiolitis is a precursor of centrilobular emphysema and may be responsible for the subtle functional abnormalities observed in young smokers. These functional abnormalities are comparable to those demonstrated in passive smokers by White and Froeb (1980) and Kauffmann et al. (1983). Taken together these studies suggest that individuals involuntarily exposed to tobacco smoke may have an increased risk of emphysema in later life. Furthermore, Tattersall et al. (1978) indicated that the maximal flow when 25% of the vital capacity remains to be expired on the flow-volume curve (comparable to the $FEF_{75-85\%}$ on the volume-time curve) appears to be one of the most promising adjuncts to the FEV_1 as a measure of early airflow obstruction in middle age smokers and as a possible predictor of future disability due to advanced disease if smoking continues. However, the actual predictive validity of this pulmonary function test still requires direct assessment by follow-up of a large sample of middle age smokers for 10 or more years.

Recently, Molotoky (1984) referred to the as yet unpublished results of Hirayama of a long term prospective study in Japan which demonstrate that nonsmoking wives exposed passively to cigarette smoke because of their husbands smoking habits, have a slightly greater incidence of chronic bronchitis and emphysema compared to nonsmoking women whose husbands don't smoke. Hence, these results would be consistent with the above inferences made from published research studies.

However, it should be emphasized that the changes in flow rates due to involuntary smoking demonstrated in the studies by Kauffmann et al. (1983) and White and Froeb (1980) are quite small and are not considered indicative of serious disease. Hence it is important to note the distinction between the statistical significance and the clinical significance of the changes in pulmonary function thought to be associated with passive smoke exposure.

Cancer

Cigarette smoke contains several carcinogens, and active smoking is known to cause a variety of different cancers such as cancers of the oral cavity and pharynx, esophagus, pancreas, respiratory tract and urinary tract. No threshold level of exposure to cigarette smoke for the development of cancer has been definitely established. This absence of a clear threshold raises the issue of whether passive smoking may also produce an increased risk of lung cancer and possibly other types of cancer.

Wynder and Hoffmann (1967) demonstrated that sidestream smoke condensate is more tumorigenic per unit weight in mouse skin assays than mainstream smoke condensate. Also involuntary inhalation of cigarette smoke has been shown by Holland et al. (1963) to produce tracheobronchial epithelial metaplasia and dysplasia in rabbits. However, these changes occurred at levels of secondhand smoke exposure which were substantially higher than those usually encountered by humans at home or work.

Bos et al. (1983) have shown that exposure of humans to secondhand smoke resulted in an increase in the urinary excretion of mutagens as measured by the Ames test. These results indicate systemic exposure to mutagens due to passive smoking.

Several epidemiologic studies have been published since 1981 which have investigated the relationship between lung cancer and involuntary exposure to smoke.

Hirayama (1981) was the first to report an association between passive exposure to cigarette smoke and lung cancer. He carried out a prospective study designed initially to evaluate the consequences to health of various factors such as cigarette smoking, alcohol consumption,

occupation and marital status. Approximately 91-99% of the census populations of 29 health centre districts in six prefectures in Japan were interviewed and followed for determination of subsequent health status over a 14 year period (January 1966 - December 1979). The nonsmoking married women subset of the original cohort for which information was available on the smoking status of their husbands totalled 91,540. The age and occupation-standardized lung cancer mortality rates in these nonsmoking married women were analyzed according to the smoking habits of their husbands. The results are summarized in Table 12.

Table 12

Husband's Smoking Category

	Non-Smoker	Ex-Smoker or 1-19 cigarettes/day	> 20 cigarettes/day
Wive's Age-Occupation Standardized Lung Cancer Mortality Rate per 100,000	8.7	14.0	18.1
Risk Ratio	1.00	1.61	2.08

The lung cancer mortality rates standardized by age and occupation were 8.7/100,000 for women with nonsmoking husbands, 14.0/100,000 for women whose husbands were ex-smokers or smoked 1-19 cigarettes per day and 18.1/100,000 for women whose husbands smoked 20 or more cigarettes per day; the corresponding relative risks of lung cancer for women whose husbands were in these smoking categories compared to women with nonsmoking husbands were 1.00, 1.61 and 2.08 respectively. This increase in the relative risk of lung cancer in nonsmoking women as the cigarette consumption of their husbands increased was statistically significant ($p=0.00097$).

When both groups of women passively exposed to tobacco smoke were considered together (eg. women whose husbands were ex-smokers or smoked 1-19 cigarettes per day and women whose husbands smoked 20 or more cigarettes per day), the overall relative risk of developing lung cancer was 1.8 compared to nonsmoking women not passively exposed to cigarette smoke. This was about one-half of the relative risk of lung cancer Hirayama (1981) reported for active smoking in women (3.8) compared to nonsmoking women with no passive exposure to tobacco smoke.

Recently, Hirayama (1983) presented updated results of this study for two additional years of follow-up for a total follow-up period of 16 years (January 1966 - December 1981). The updated standardized mortality ratios of lung cancer in nonsmoking women were 1.00, 1.36, 1.42, 1.58 and 1.91 when husbands were nonsmokers, ex-smokers, daily smokers of 1-14, 15-19 and 20 or more cigarettes per day respectively. This trend of increasing relative risk of lung cancer with increasing involuntary exposure to tobacco smoke was statistically significant ($p=.00178$). In addition

an increased risk of cancer of the paranasal sinuses was found in nonsmoking wives exposed passively to cigarette smoke. A total of 28 cases was observed. The risk ratios were 1.00, 2.27, 2.56 and 3.34 when husbands were respectively nonsmokers, smokers of 1-14, 15-19 and 20 or more cigarettes daily. These results were also statistically significant ($p=0.01064$).

The initial results of this study generated considerable debate in the medical literature. The study was criticized by Mantel (1981) because of an apparent error in the calculation of the X^2 trend statistic. The Tobacco Institute in the U.S. (1981) claimed that this trivial arithmetical error invalidated the entire study. Although as Mantel (1981) indicated, the unstandardized results were not statistically significant, standardization by age and occupation by Harris and DuMouchel (1981) resulted in a X^2 value of 8.09 which was still statistically significant ($p=0.004$) and similar though not identical to the value of 10.88 given in the original paper by Hirayama.

The study was also criticized by Tsokos (1981) because the lung cancer rates in women were standardized for the ages and occupations of the husbands rather than the wives' and the 10 year age intervals were probably too wide to allow for good standardization for age.

After publishing the original study Hirayama (1981b) subsequently reported that in a sample of 23 necropsied cases out of the initial series of 174 lung cancers in nonsmoking women, the majority (17) were of one histologic type (adenocarcinoma). This type of lung cancer is less strongly related to smoking than are most other histologic types such as squamous cell carcinoma. Furthermore, it is known that the Japanese population has a disproportionately high percentage of adenocarcinoma compared to Western

countries. MacDonald (1981) mentions that the proportion of adenocarcinoma of the lung compared to other histologic types of lung cancer in Japan is approximately twice as high as in any of the developed countries of the world and this suggests the presence of factors other than smoking which may be specifically related to the development of adenocarcinoma. Recent evidence of trends in lung cancer rates in Japan also suggests that there may be other, as yet unidentified, etiologic factors related to lung cancer. Before the Second World War lung cancer was a relatively rare disease in Japan. However, during the period 1947-78 female lung cancer rates rose nine-fold and yet Hirayama's results show only a four-fold relative risk (RR=3.8) in active female smokers compared with female nonsmokers not passively exposed to cigarette smoke. Furthermore, the prevalence of smoking in Japanese women is quite low (about 15%).

Trichopoulos et al. (1981) carried out a case control study in Greece which corroborated Hirayama's findings. They identified 51 Caucasian female lung cancer patients and 163 adult female controls who were orthopedic patients admitted to hospitals in Athens during the period September 1978 to June 1980. The cases and controls were similar in terms of the distribution of various potential confounders such as age, duration of marriage, occupation, socioeconomic status and recent residence. All cases and controls were interviewed regarding their smoking habits and those of their husbands. It appears that the interviewer was not blinded to the disease status of the patients being interviewed. Among the 51 women with lung cancer, 11 were smokers, whereas among the 163 controls 14 were smokers giving an odds ratio or relative risk estimate of 2.9 associated with active smoking. There were therefore 40 nonsmoking cases and 149 nonsmoking controls from the original sample. Table 13 shows the distribution of nonsmoking women with lung cancer and of nonsmoking controls according to the smoking habits of their husbands.

Table 13

Smoking Habits of Husbands of Non-Smoking Women with Lung Cancer and of Non-Smoking Control Women

Diagnostic Group	Non-smokers	Ex-smokers	Cigarettes per Day (current smokers) 1-10	11-20	21-30	31+	Total
Lung cancer	11	6	2	13	4	4	40
Controls	71	22	9	32	6	9	149
RR Estimate (Odds Ratio)	1.0	1.8	2.4		3.4		

The table clearly demonstrates that the relative risk estimate (odds ratio) of lung cancer increases with increasing cigarette consumption by the husband. The odds ratios were 1.0, 1.8, 2.4 and 3.4 for the husbands' smoking categories: non-smokers, ex-smokers, current smokers 1-20 cigarettes per day, current smoker 21 or more cigarettes per day respectively. The X^2 for linear trend was significant ($p<0.02$). Also when the husbands smoking behaviour was categorized according to the estimated total number of cigarettes smoked, the same statistically significant relationship was observed in nonsmoking women between increased estimated risk of lung cancer and total number of cigarettes smoked by the husband.

The study has been criticized because:

(a) many (35.3%) of the tumours lacked histological confirmation

(b) the cases and controls were obtained from different hospitals and,

(c) there was a small number of subjects, particularly cases.

Subsequently, Trichopoulos et al. (1983) reported updated results of the first study with the number of cases and controls increased by approximately 100% and 50% respectively. There were 77 cases and 225 controls for this second analysis. The smoking habits of the husbands of nonsmoking women with lung cancer and of nonsmoking control women are outlined in Table 14.

Table 14

Smoking Habits of Husbands of Non-Smoking Women with Lung Cancer and of Non-Smoking Control Women

Diagnostic Group	Non-smokers	Ex-smokers	Cigarettes per Day (current smokers)				
			1-10	11-20	21-30	31+	Total
Lung cancer	24	15	2	22	7	7	77
Controls	109	35	16	40	8	17	225
RR Estimate (Odds Ratio)	1.0	1.9	2.4		3.4		

These results are similar to those obtained in the initial phase of the study. Once again the odds ratio or relative risk estimate of lung cancer in nonsmoking women increased with the smoking habits of the husband. As mentioned, these results were based on a larger number of cases and controls than in the original study and the X^2 for linear trend was larger with a smaller p value ($p<.01$) for these updated results.

Correa et al. (1983) also carried out a case-control study to investigate the relationship between passive exposure to tobacco smoke and lung cancer. A total of 1,338 lung cancer patients and 1,393 controls were identified from admission and pathology records of several participating hospitals in 29 Louisiana counties. Histologic confirmation was obtained for 97% of the cases. Patients with bronchioalveolar carcinoma were excluded; however patients with adenocarcinoma were included in the study. For each case, a control was randomly selected from patients attending the same hospital and matched for race, sex and age (within 5 years). Patients with other smoking-related cancers or diseases were excluded from the control group.
The cases and controls or their next of kin were interviewed to determine the smoking habits of the cases/controls, their spouses and their parents. Nonsmokers with lung cancer and nonsmoking controls were identified and the smoking histories of their spouses were compared. Only 10 of the 1,036 male cases were ever-married nonsmokers; there were 25 nonsmoking, ever-married women with lung cancer out of 302 female cases. For one female and two male nonsmoking patients no information was available on the smoking history of the spouse; two female patients' husbands were smokers but the amount and duration were unknown. These cases were therefore excluded from analysis leaving 8 male and 22 female cases.

The relationship between the nonsmoking, ever-married men and women according to total lifetime pack-years smoked by their spouses is described in Table 15.

Table 15

Non-Smoking, Ever-Married Lung Cancer Cases and Controls and Lifetime Consumption of Cigarettes by their Spouses

	Cigarettes Smoked by Spouse (pack years)		
	None	1-40	>41
Males			
Cases	6	2	0
Controls	154	20	6
Odds ratio	1.0		
		2.0	
Females			
Cases	8	5	9
Controls	72	38	23
Odds ratio	1.0	1.18	3.52*
		2.07	
Both sexes			
Odds ratio (adjusted for sex)	1.0	1.48	3.11*

*$p<0.05$

The odds ratio or relative risk estimate of lung cancer from smoke exposure due to smoking by a spouse was increased when the spouse was a heavy smoker (> 41 pack years). The odds ratio of 3.52 for women whose husbands smoking category was equal to or greater than 41 pack years was statistically significant as was the odds ratio of 3.11 for both men and women whose spouses' smoking category exceeded 41 pack years.

Correa et al. (1983) did not carry out a X^2 linear trend analysis. However such an analysis could be done from their reported data. When the calculations for X^2 linear trend were carried out the results were as follows:

	X^2 Linear Trend	P Value
Males	.18648	.05
Females	5.15984	<.05
Males & Females	12.64193	<.05

Hence a significant trend of increasing lung cancer rates with increasing passive exposure to cigarette smoke can be demonstrated for females and males plus females. These results are therefore similar to those of Trichopoulos et al. However, it must be emphasized that the study by Correa et al. had a small number of nonsmoking subjects with lung cancer (30).

For active smokers, similar calculations of odds ratios or relative risk estimates of lung cancer and smoking category of spouses did not show an increased risk associated with the smoking of spouses except for light smoking men (less than 20 pack-years) who had a relative risk of 1.5 when married to women who were heavy smokers (41 pack years or more). Hence, for smoking subjects, the strong influence of active smoking overshadowed any effect on lung cancer due to passive smoking.

The relationship between lung cancer and passive exposure due to parental smoking was also examined in all cases and controls (smokers and nonsmokers). In this study smoking habits in cases and controls were found to be related to the smoking habits of their parents. Heavy smokers were more likely than the other patients to have had smoking parents. Similarly, heavy smokers were also more likely to have lung cancer. Hence, active smoking in the cases and controls had to be controlled before a valid comparison of parental smoking in cases and controls could be done. Therefore a logistic regression analysis was carried out with the inclusion in the logistic regression model of several variables indicative of active smoking. From the logistic regression analysis, the relative risk estimate associated with maternal smoking was 1.36 ($p<0.02$) for both sexes and 1.5 ($p<0.01$) for males. No increase in risk of lung cancer was found in this model for female subjects whose parents smoked or for male subjects whose fathers smoked. The risk was significantly raised only in male smokers whose mothers smoked. However, it is not clear whether the results reflect a true effect associated with maternal smoking or the inability to control completely for active smoking.

Garfinkel (1981) using data collected by Hammond in a 12 year prospective study of lung cancer (1960-1972) by the American Cancer Society, was unable to corroborate the results of Hirayama (1981, 1983), Trichopoulos et al. (1981, 1983) and Correa et al. (1983). In Garfinkel's analysis a total of 176,739 nonsmoking women were identified and lung cancer mortality in women who were married to cigarette smokers was compared with the mortality in women married to nonsmokers. The results of the analysis are presented in Table 16.

Table 16

Observed Versus Expected Lung Cancer Deaths
Among Nonsmoking Women according to the
Smoking Habits of their Husbands

	Husband did not smoke	Husband smoked <20 cigarettes/ day	Husband smoke ⩾20 cigarettes/ day
Observed deaths	65	39	49
Expected deaths	65.00	30.67	44.67
Mortality ratio	1.00	1.27	1.10

Expected numbers of deaths were based on the lung cancer death rates for the 12-year period 1960-72 by 5-year age groups of the women with nonsmoking husbands.

The observed versus expected lung cancer mortality ratio for women whose husbands smoked less than 20 cigarettes a day was 1.27. For women whose husbands smoked 20 or more cigarettes a day it was 1.10. Neither of these mortality ratios was statistically significant. This initial analysis did not take into account various possible confounding factors. Therefore, a second analysis was carried out after pairs of women were matched for age, race, education, residence and husband's occupational exposure. After this adjustment for potential confounders, the ratio of lung cancer deaths in women whose husbands smoked less than 20

cigarettes a day to those in women whose husbands never smoked was 1.37. The comparable ratio for women whose husbands smoked 20 or more cigarettes a day was 1.04. Again, neither of these differences was statistically significant.

Therefore, this study found slightly increased rates of lung cancer in women whose husbands smoked compared to women whose husbands did not smoke, but the results were not statistically significant. Furthermore, the dose-response results did not support a causal association - the risk of lung cancer appeared to diminish as the number of cigarettes smoked by the husbands increased.

One of the major methodologic problems with this study was that Garfinkel analyzed data from another study that was not specifically designed to answer the question of whether passive exposure to cigarette smoke increases the risk of lung cancer. This ex post facto hypothesis testing did not allow for proper data collection procedures to answer the question in a valid and efficient manner. For example, the husband's smoking history was available for only 27.1% of the nonsmoking wives with lung cancer (153 out of 564). The Hirayama study had a much higher percentage of husbands' smoking histories available for the nonsmoking wives.

Another recent epidemiologic study by Chan and Fung (1982) in Hong Kong did not demonstrate a statistically significiant relationship between involuntary exposure to tobacco smoke and lung cancer in women. In this case control study it was found that, among nonsmoking women, the proportion of lung cancer cases whose husbands smoked was slightly lower than that of controls (34 of 84 or 40.5% versus 66 of 139 or 47.5%). Hence the estimated risk of lung cancer was actually lower (Odds Ratio = 0.75) in the nonsmoking wives of smokers than in nonsmoking women who husbands didn't smoke.

Koo et al. (1983) also did not find a statistically significant association between lung cancer and passive smoking in another case control study in Hong Kong. In this study 56 nonsmoking female lung cancer cases and 85 nonsmoking female controls were compared in terms of the average duration of previous exposure to secondhand tobacco smoke at work and at home. Lung cancer cases had an average exposure to secondhand smoke that was 3.8 years greater than that of controls but the difference was not significant.

Miller (1984) carried out a cross-sectional analytic survey of recently-deceased nonsmoking women identified by death notices in an Erie County Pennsylvania newspaper during a 20 month period. Of 4,130 deceased individuals (both men and women) interviews with surviving relatives were obtained on only 1,838. From this total of 1,838 individuals, 537 nonsmoking recently-deceased women were identified. These women were categorized according to: (1) cause of death (either cancer or not cancer), and (2) husband's smoking status (smoker or nonsmoker). When the odds of having a husband who smoked were compared for nonsmoking women with and without lung cancer, the results showed an odds ratio or relative risk estimate of lung cancer due to secondhand smoke from their husband's smoking of 1.4. This result was not statistically significant. Subgroup analysis was carried out according to whether or not the women were employed outside the home. Those women who worked would also be exposed to secondhand smoke in the workplace and this exposure could confound the association between cancer and secondhand smoke in the home. For the entire group of women who did not work outside the home, the relative risk estimate of cancer due to their husband's smoking was 1.94 and this result was statistically significant ($p<0.02$). For employed women the corresponding relative risk estimate was a non-signficant 0.8.

Kabat and Wynder (1984) carried out a case-control study of the relationship between several different exposure variables, including passive smoking, and lung cancer in nonsmokers. Nonsmoking lung cancer cases were obtained from several hospitals most of which were located in New York City. Controls were selected from several hospitals in the same area; all controls had been hospitalized for non-tobacco-related disorders. All subjects were interviewed in hospital using a standardized questionnaire which included questions on secondhand smoke exposure at home and at work and whether the spouse smoked. Separate subgroup analysis was done for males and females according to each of the above three indexes of secondhand smoke exposure, a total of 6 separate subgroups (2 x 3). For the 25 male cases and 25 controls there was a statistically significant difference in the proportion of lung cancer cases reporting exposure to secondhand smoke at work. Eighteen of the 25 cases reported having been exposed to cigarette smoke at work compared to 11 of 25 controls, giving an odds ratio of 3.3 ($p<0.045$). However neither of the other two subgroup analyses in the men and none of the three subgroup analyses in the 53 lung cancer female cases and 53 female controls showed a relationship between lung cancer and secondhand smoke exposure. The multiple subgroup analysis carried out in this study resulted in an increase in the likelihood of a type I or α error (rejecting the null hypothesis of no effect due to passive smoking when the null hypothesis is true). For example when six subgroup analyses are carried out, as in this study, the overall likelihood of a type I error is:

$$P(\text{type I error}) = 1 - (1 - \alpha)^n$$

$$= 1 - (1 - .05)^6$$

$$= .265$$

where n = number of subgroup analyses.

α = level of significance for each analysis.

Hence studies such as this case control study of Kabat and Wynder (1984) that carry out multiple subgroup analyses with no adjustment for the level of significance used in each subgroup analysis are quite likely to find an association between passive smoking and lung cancer in one of the subgroups by chance alone.

Gilles et al. (1984) have reported preliminary results of a prospective study in Scotland comparing lung cancer rates in groups with and without domestic secondhand smoke exposure. Elevated rates of lung cancer have been found in men (relative risk = 3.25) but not in women. However, Gilles et al. state that no firm conclusions can be drawn as yet because insufficient time has elapsed since the beginning of this prospective study.

Sandler et al. (1985a, 1985b, 1985c) reported the results of a large case control study which examined the possible association between various types of cancer and secondhand smoke. The overall cancer risk in adulthood due to secondhand smoke exposure was examined using smoking by the spouse as the index of passive smoking (1985a). Cases were selected from a hospital-based tumour registry at the North Carolina Memorial Hospital and included all sites except basal cell cancer of the skin. Age, sex and race matched controls were selected from friends of the cases (60%) or by systematic telephone sampling. Information on smoking by the spouse and other relevant variables was obtained for 518 cancer cases and 518 noncancer controls. Estimated overall cancer risk (odds ratio) among individuals ever married to smokers was 1.6 times that among those never married to smokers. This increased risk was statistically significant ($p<0.01$) and the significance remained after adjustment for relevant potential confounders. Subgroup analysis for various cancer sites indicated that statistically

significant estimated relative risks were found for several specific cancer sites (breast, cervix, female genital system, endocrine system) and were not limited to active smoking-related cancers. Only 22 lung cancer cases were included in this study and the estimated risk of lung cancer due to passive smoking was not statistically significant (odds ratio = 1.9, $p>0.05$). Therefore this study suggested that there was an association between secondhand smoke exposure and a broad spectrum of cancer, rather than just lung cancer.

Sandler et al. (1985b) also used data from this case control study to examine the cancer risk in adulthood from early life exposure to parents' smoking. Information on the smoking habits of parents was obtained for 438 cancer cases and 470 controls. There was a statistically significant relative risk estimate of 1.5 for all cancer sites among individuals whose fathers smoked in the household. Adjusting for potential confounders such as individual smoking status, smoking by spouse and maternal smoking did not alter this finding. The relative risk estimates, for both smoking-related (1.6) and nonsmoking-related (1.4) cancers and paternal smoking were also statistically significant. In addition specific cancer sites with elevated relative risks due to paternal smoking included cervix, brain and hematopoietic tissue. However there was no statistically significant difference between cases and controls in reported exposure to maternal smoking. This lack of association persisted after adjustment for potential confounding factors. Despite the small number of lung cancer cases included in this study, Sandler et al. (1985b) also discussed the relation between lung cancer risk and parental smoking because of the current interest in passive smoking and cancer risk at this site. The relative risk estimate for lung cancer among individuals whose fathers smoked was 2.5 after adjusting for age and individual

smoking. The adjusted relative risk estimate associated with maternal smoking was 1.8 but this was based on only two smoking mothers among 15 cases. Neither of these relative risk estimates of lung cancer from exposure to secondhand smoke due to parental smoking was significant.

Sandler et al. (1985c) also analyzed the results of this case control study in terms of the relationship between lung cancer and cumulative lifetime exposure to secondhand smoke due to smoking by spouses, parents, and other childhood household members. Analysis was restricted to individuals who lived with both natural parents for most of the first 10 years of life. Results were reported for 369 cases and 401 controls who supplied information about the smoking habits of their spouses, parents and other household members. When analyzed by a χ^2 linear trend test, overall cancer risk rose steadily with each additional household member who smoked over an individual's lifetime ($p<0.01$). Cancer risk was also greater for individuals with exposure to secondhand smoke during both childhood and adulthood than for individuals with exposures during only one period. These statistically significant trends were observed for both smoking-related and other cancer sites and constitute evidence of dose-response between overall cancer rates and secondhand smoke exposure. No statistically significant trend was found for cancer of the respiratory tract in nonsmokers and increasing number of smokers in the household. However, only 19 respiratory tract cancers were included in this analysis and therefore the statistical power of this subgroup analysis was quite low.

The initial series of studies during the period 1981-83 yielded results which did not allow for definitive determination of causality of lung cancer due to passive smoking. For example, the office of the U.S. Surgeon General (1982) reviewed the evidence relating lung cancer to

passive exposure to tobacco smoke from three of the initial studies (Hirayama, 1981; Trichopoulos et al., 1981; and Garfinkel, 1981) and concluded that a causal relation could not be assumed from the results of these studies. The Ontario Medical Association (1983) prepared a position statement on health effects from secondhand tobacco smoke which stated that there is suggestive evidence that long-term exposure to secondhand tobacco smoke increases the risk of lung cancer. A number of other reviews of the health effects of secondhand tobacco smoke have been published (Lee, 1982; Task Force on Smoking, Ontario Council of Health, 1982; Lefcoe et al., 1983; Weiss et al., 1983; Spengler and Soczek, 1984). In all these reviews the term suggestive or a comparable term is used to describe the relation between lung cancer and secondhand tobacco smoke. Recently Repace and Lowrey (1985) reviewed the existing research results and concluded that there is sufficient evidence to assume a causal relationship between lung cancer and passive smoking.

This controversy regarding causality of lung cancer from secondhand tobacco smoke may be clarified to some extent by applying a set of criteria or rules of causation to the existing epidemiologic studies. Hill (1971) has developed a set of criteria for causation and these have been applied to questions of causation in occupational epidemiology by Sacket (1980) and the Advisory Council on Occupational Health and Safety, Ministry of Labour (1983). The International Agency for Research on Cancer (IARC) has a short list of the four main criteria for determining causality of putative carcinogens. These criteria include: (1) the consistency of studies using different design architectures and conducted in different geographic areas (2) the strength of the association (eg. relative risk) (3) the presence of a dose-response relation and (4) the demonstration of a reduction in cancer incidence with a reduction in exposure to the putative carcinogen.

Evidence for criterion (4) would require demonstration (preferably from a prospective study) of a reduction of lung cancer rates in passive smokers when their passive smoking is reduced or eliminated. No good published evidence of this kind is available at present. However a reduction in lung cancer incidence after reduction of smoking has been found for active smoking (Office of U.S. Surgeon General, 1982). The strength of the association between passive smoking and lung cancer is much less than that for active smoking and lung cancer. The relative risk estimates in most of the passive smoking studies cited are in the range of 1.5 to 3.0 with an average value of about 2. This relative risk is much lower than the relative risk of about 10 - 20 for active smoking. As mentioned in this review, several of the studies show evidence of a dose-response relation between passive smoking and lung cancer. Hence the key remaining criterion for determining causality is the consistency of the study results.

Of the twelve studies reviewed (Hirayama, 1981; Trichopoulos et al., 1981; Correa et al., 1983; Garfinkel, 1981; Chan and Fung, 1982; Koo et al., 1983; Gilles et al., 1984; Miller, 1984; Kabat and Wynder, 1984; Sandler et al. (1985a, 1985b, 1985c), the majority found an association between passive smoking and lung cancer although in some cases multiple subgroup analysis was required to demonstrate an association (eg. Kabat and Wynder 1984), and in others overall cancer was considered rather than lung cancer (Sandler et al., 1985a, 1985b, 1985c). Also a publication bias (Pocock, 1985) tends to favour publication of studies that find an association rather than those that do not, especially for studies of very topical issues. This type of bias may be operative in the reporting and publishing of passive smoking studies. However, the studies reviewed appear to show overall consistency of an associtition between lung cancer and passive smoking.

Therefore a review of the existing published epidemiologic studies and the application of criteria of causation to these study results indicates that the evidence does suggest that lung cancer is caused by long-term exposure to secondhand tobacco smoke. This conclusion is also biologically plausible given the proven association between lung cancer and active smoking, the demonstrated presence of several carcinogens, including lung carcinogens, in sidestream tobacco smoke, and the general acceptance that the risk of lung cancer is directly related to the amount of tobacco smoke inhaled. In addition further studies will probably help to clarify the question of overall consistency of study results.

In most of the studies reviewed, the index of passive smoking was the spouse's smoking habits. However, this index is likely to be inaccurate. The husband smokes only a portion of his cigarettes at home; furthermore, there is likely to be considerable variability in the percentage of cigarettes smoked at home. Also, the wife may be exposed to other sources of passive smoking aside from her husband's smoking. Friedman et al. (1983) have suggested that although traditional Greek and Japanese wives' passive smoking may have depended almost entirely on their husbands' smoking habits, American spouses' smoking habits appear to be an inaccurate index of passive smoking. Divorce rates are higher in the U.S. and hence the smoking status of the husband at the start of a prospective study may not be indicative of actual passive exposure to tobacco smoke after several years have elapsed; similarly in a retrospective case control study, determination of the present smoking status of husbands may not reflect the actual secondhand smoke exposure that existed previously. Also a greater percentage of women work in the U.S. than in Japan or Greece and hence they are passively exposed to smoke in the work environment as well as in the home. Indeed, Repace (1984)

has reanalyzed the results of Garfinkel's study and found that these results may not be inconsistent with the Hirayama study if a correction is made for passive exposure at work as well as at home.

Accurate determination of smoking status in individuals and their spouses as well as determination of tobacco smoke exposure in the work environment and thorough follow-up to determine consistency of smoking category as well as work exposure are needed. In addition, validation of the index of passive smoking by correlation with air sampling results or biologic monitoring results should be done. Such factors would be important components of a study on a large group of subjects designed specifically to answer the question of whether passive exposure to tobacco smoke is associated with lung cancer.

Repace and Lowrey (1985) recently carried out a risk assessment of lung cancer due to secondhand tobacco smoke exposure. They attempted to quantify the lung cancer mortality likely to occur given specified levels of tobacco tar exposure from secondhand tobacco smoke. These risk assessments are needed before risk management interventions can be evaluated to determine the health impact of various possible interventions. Prior to their estimations of the lung cancer risk from secondhand smoke, Repace and Lowrey reviewed the studies that have been carried out to investigate the relation between lung cancer and passive smoking, and concluded that the criteria for causality described by the International Agency for Research on Cancer (IARC) had been met.

Their risk assessment involved comparing the dose of tobacco tar from secondhand smoke exposure and lung cancer response information that had been obtained from different studies. This type of dose-response estimation is referred to as a phenomenologic dose-response relation. The dose estimation was obtained from Repace and Lowrey's own work. They carried out laboratory measurements to estimate the average tobacco tar exposure for home and work environments. This exposure information was combined with estimates of the probabilities of nonsmokers being exposed to secondhand tobacco smoke at home and/or at work, to obtain a probability-weighted average exposure to secondhand smoke of 1.43 mg tobacco tar per day. These calculations are summarized in Table 17.

Table 17

ESTIMATED PROBABILITIES OF NONSMOKERS EXPOSURE
TO TOBACCO SMOKE
AT HOME AND AT WORK
After Repace and Lowrey, (1983)

Non-exclusive probability of being exposed at work:	63%
Probability of <u>not</u> being exposed at work:	37%
Non-exclusive probability of being exposed at home:	62%
Probability of <u>not</u> being exposed at home:	38%

Location	Daily Average Probability of being exposed (Rounded Values)	Exposure (mg) Modeled Daily Average	Exposure (mg) Daily Probability Weighed Value
At work and at home: %	63 x 62 = 39	2.27	0.89
Neither at work nor at home: %	37 x 38 = 14	0.00	0.00
At home but not at work: %	62 x 37 = 37	0.45	0.10
At work but not at home: %	63 x 38 = 24	<u>1.82</u>	<u>0.44</u>
	Total: % 100		1.43

(The estimated exposure to tobacco tar from secondhand tobacco smoke for U. S. adults of working age, at work and at home determined from average concentrations of tobacco tar calculated for model workplace and home microenvironments and weighted for average occupancy).

The response information was obtained from studies by Phillips et al. (1980a, 1980b) that compared lung cancer mortality rates in nonsmoking Seventh Day Adventists in Southern California and nonsmokers in the general Southern California population. Seventh Day Adventists have rigorous proscriptions against the use of tobacco. Hence Seventh Day Adventists are probably less likely than the general population to be involuntarily exposed to tobacco smoke at home or in the workplace, because Seventh Day Adventists' homes and business are likely to be places where smoking is not permitted, and because the great majority of Seventh Day Adventists' social contacts are among other Seventh Day Adventists who do not smoke. Therefore, the excess lung cancer rates in nonsmokers in the general population compared to nonsmoking Seventh Day Adventists is presumed by the authors to be due mainly to passive smoking. However, the groups being compared may differ in a variety of other characteristics that may affect reported lung cancer rates such as access to medical care, occupational exposure to airborne carcinogens and other factors.

Repace and Lowrey (1985) carried out a calculation based on the age-standardized difference in lung cancer mortality rates between Seventh Day Adventists who never smoked and demographically comparable non Seventh Day Adventists who never smoked (aged > 35 years) to yield an estimated 4700 lung cancer deaths per year for the 62.4 million nonsmokers in the United States aged > 35 years. Therefore, 7.4 lung cancer deaths per 100,000 person-years were attributed to passive smoking. Finally, using the attributable risk of 7.4 lung cancer deaths per 100,000 person-years and dividing by the estimated average exposure to tobacco tar of 1.43 mg/day, Repace and Lowrey (1985) estimated a phenomenological dose-response relation for the general U.S. poulation at risk (nonsmokers aged > 35) of about 5 lung cancer deaths (7.4/1.43) per 100,000 person-years per mg/day tobacco tar exposure.

Repace and Lowrey also estimated the lung cancer rates for passive smokers by extrapolation of a dose-response curve for active smokers to the average levels of tobacco tar exposure of passive smokers (1.43 mg/day). This resulted in an estimate of 0.60 lung cancer deaths per 100,000 person-years per mg/day of tobacco tar due to passive smoking. Hence this estimate was more than one order of magnitude lower than the original estimate using lung cancer data from Phillips et al. (1980a, 1980b).

Therefore a sensitivity analysis was carried out to compare the predictions of lung cancer death rates due to secondhand smoke exposure from (a) the phenomenologic dose-response relation and (b) extrapolation from active smoking. These two prediction methods were compared in terms of how well their estimates of lung cancer death rates due to passive smoking could predict the relative risks and overall lung cancer death rates for both the Garfinkel Study in the U.S. (1981) and the Hirayama Study in Japan (1981). It was assumed by Repace and Lowrey (1985) that the nonexposed group in Garfinkel's study also included individuals exposed to secondhand smoke at work, whereas in the Hirayama study the nonexposed group was assumed not to have any "tainted" controls. Given these and other assumptions, the phenomenologic dose-response method was found to be a better predictor than the active smoking extrapolation method for both relative risk and overall lung cancer death rates in both the Garfinkel study and Hirayama study. Therefore the phenomenologic dose-response was concluded to be a better predictor of lung cancer death rates due to passive smoking. As mentioned before, this method predicted a risk of about 5 lung cancer deaths per 100,00 person-years per mg/day tobacco tar exposure due to passive smoking in nonsmokers aged > 35 years.

CONCLUSION

It has been estimated that about 63% of nonsmokers are passively exposed to tobacco smoke at work and that 86% of nonsmokers are passively exposed to tobacco smoke in either the work or home environment or both. Passive smokers are exposed to much lower concentrations of tobacco smoke than active smokers and most of the constituent chemicals of the smoke are the same, although the constituents may differ in relative proportions in secondhand smoke compared to the smoke to which active smokers are exposed. Comparisons of various biological monitoring results in active and passive smokers indicate that passive exposure over an eight hour workday in an office environment where many people smoke is probably comparable to light active smoking (ie. about 1-5 cigarette equivalents).

There is little doubt about the irritating and annoying effects of secondhand tobacco smoke. Also, the evidence appears quite convincing for the exacerbation of the symptoms of some diseases, especially allergic rhinitis, asthma and angina due to passive smoking. Similarly, the evidence indicates that, in children, increased frequency of pulmonary symptoms such as chronic cough and increased rates of acute respiratory infection as well as decrements in various pulmonary function tests are associated with exposure to parental (mainly maternal) smoking. The existing research on changes in pulmonary function tests ($FEF_{25-75\%}$ and $FEF_{75-85\%}$) indicative of small airways impairment in adults exposed passively to cigarette smoke for many years is more equivocal but on balance seems to favour the occurrence of such changes. The overall evidence from currently available published epidemiologic studies does suggest that a small increased risk of lung cancer may be associated with long-term exposure to secondhand tobacco smoke. This conclusion is also biologically plausible given

the proven association between lung cancer and active smoking, the demonstrated presence of several carcinogens, including lung carcinogens in sidestream tobacco smoke, and the general acceptance that the risk of lung cancer is directly related to the amount of tobacco smoke inhaled.

Therefore various health effects have been demonstrated to be due to involuntary exposure to tobacco smoke. However the health hazard to an individual or a group of individuals in a particular work environment would depend on the actual exposure conditions. These exposure conditions are a function of a number of factors such as the size of the room, the ventilation rate, the percentage of fresh make up air supplied, the number of smokers in the room, the total number of cigarettes smoked, the rate and manner of smoking and the type of cigarettes. For these reasons, although it is difficult to quantify the health hazard on an individual basis, it is recommended that long-term exposure to secondhand tobacco smoke in the workplace should be minimized or avoided.

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